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Original Articles and Clinical Cases.

DEGENERATIONS FOLLOWING LESIONS OF THE RETINA IN MONKEYS.

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THE optic nerve, so-called, consists of centripetal and centrifrugal fibres, of which the former are probably the more numerous. Of these, most are believed to be the axons of the ganglion-cells in the retina. If therefore, groups of the ganglion-cells are destroyed, we should expect to find the corresponding fibres of the optic nerve degenerated, and to be able to trace these fibres to their ultimate destinations in the brain. This line of research has hitherto received very scanty attention.

Falchi (1) in 1886, and Baquis (2) in 1889, made retinal lesions for the purpose of studying the reaction of the different retinal elements.

Pick (3) in 1895, destroyed circumscribed areas of the retina in a very large number of rabbits, and traced the degenerations in the optic nerves, chiasma and tracts. He arrived at the following conclusions:—"The fibres retain, throughout their whole course, both in the optic

nerve and in the optic tract, the same relative position; the crossing in the chiasma occurs in regular sequence: first the innermost bundles of the optic nerve, and then successively those lying farther outwards; definite parts of the transverse section of the optic nerve thus correspond to definite parts of the tract of the opposite side. To the lower parts of the optic nerve answer similarly the parts lying below in the tract; to the inner parts of the optic nerve, the outer parts of the tract; to the outer parts of the optic nerve, the inner parts of the tract; as also it is probable that the upper parts of the tract correspond to the upper part of the nerve. In the chiasma, there is merely a decussation of fibres in the transverse direction, and not any rearrangement of them in the vertical direction. The topographical relations between the retina and the optic nerve can be defined thus:—The different parts of the optic nerve correspond in general to the similarly situated parts of the retina; and in a similar manner, the relations between the retina and tract of the contralateral side are in accordance with the same arrangement."

As in the earlier researches of von Gudden, the small direct tract which exists in the rabbit seems to have escaped Pick's observation. Pick made one or two observations upon cats, with the same results.

Dean and Usher (4), independently, in the same year, arrived at similar conclusions with regard to the optic nerve in rabbits. They do not record any investigations of the chiasma or tracts. They also made a lesion between the disc and the macula in a monkey, and obtained degeneration in the papillo-macular bundle in the optic nerve. The degeneration was similar in distribution to that found in cases of toxic amblyopia, viz., a wedge-shaped area on the temporal side near the eye, becoming crescentic and nearer the centre of the nerve farther back, and finally central near the chiasma.

Method.

In my experiments operations were performed upon six monkeys. The pupils having been previously well dilated by the instillation of atropine, the animal was anæsthetised

with ether. The fundus was examined ophthalmoscopically to see that it was normal, and the conjunctival sac was washed out with weak solution of perchloride of mercury. A speculum was inserted, and the eye fixed by fixation-forceps, held by an assistant. A Graefe's cataract knife was then introduced into the eye 4 or 5 mm. behind the corneo-scleral margin, at either the nasal or temporal side, thus avoiding dangerous injury to the ciliary body, and minimising injury to the retina. The knife was passed across the eye through the vitreous to the opposite side, and the retina wounded there to the required extent, the position of the point of the knife being in some cases observed by the ophthalmoscope (direct method). The ophthalmoscope was especially used in lesions near the disc or macula. In other cases, the wound was made without ophthalmoscopic examination, the slight resistance encountered being sufficient to show that the retina had been reached. The exact position and nature of the wound were subsequently determined by ophthalmoscopic examination, which was repeated after an interval of a few days, and also shortly before killing the animal. The lesions were all investigated microscopically by a suitable section of the eye, *post mortem*, and were then prepared for microscopic examination. The results of the latter investigation have elicited several points which are of ophthalmological rather than neurological interest, and will be detailed elsewhere.

There was usually no loss of vitreous during the operation, but a small bead escaped in two cases, without, however, causing any untoward result. The wound of entrance healed with great rapidity in all cases. There was slight hyperæmia of the conjunctiva for a day or two, but this quickly passed off, and the animal looked perfectly normal.

The monkeys were chloroformed to death from a fortnight to three weeks after the injury. The brain was removed and placed in formol, the optic nerves being cut through immediately in front of the chiasma. The roofs of the orbits were then removed, and the optic nerves dissected free from the other orbital contents. Great care was taken

to preserve the accurate orientation of the nerves. The eyes were left *in situ* until the orbits had been dissected back to the foramina, so that the nerves were thus anchored at each end. The eyes, with the nerves attached, were then lifted out of the orbits and pinned out upon a piece of cork. They were then hardened in formol. When hardening was completed, the eyes were removed and examined. The nerves were pinned out, side by side, upon a piece of liver, and transferred, after thorough washing in running water, to Busch's solution. In this condition they were put through the alcohols and embedded in celloidin, the pins being removed after the celloidin had set. Small, fine, entomological pins were used. There was usually a slight reduction of osmium around the pin-holes, but this did not extend for any distance into the nerve, and the degenerations were determined from careful examination of many sections, and not from isolated ones. The sections were cut with a Jung microtome, every fifth (in some places, *e.g.*, the chiasma, more) being mounted and examined.

Experiments.

Experiment I.—Rhœsus. Right Eye.

October 16, 1901. A small lesion, about 2 mm. long, in a direction tangential to the disc, was made near the equator in the lower nasal quadrant. There was a little hæmorrhage; the area of pigmentary degeneration was very little larger than the lesion.

October 31, 1901. Killed.

The degenerations in the optic nerve are shown in the micro-photographs on Plate I. The degenerations in the optic nerve, chiasma and tracts are shown diagrammatically in figs. 1 to 8. (The outlines of the diagrams were all drawn with the Edinger Projection Apparatus, the details being filled in free-hand, under a higher power, only degenerations which could be traced along the nerve being drawn. The diagrams therefore represent what are believed to be the essential degenerations following the given lesion.)

Figs. 1 to 5 show that the main area of degeneration is wedge-shaped near the eye, the apex of the wedge being

PLATE I.

FIG. 1.

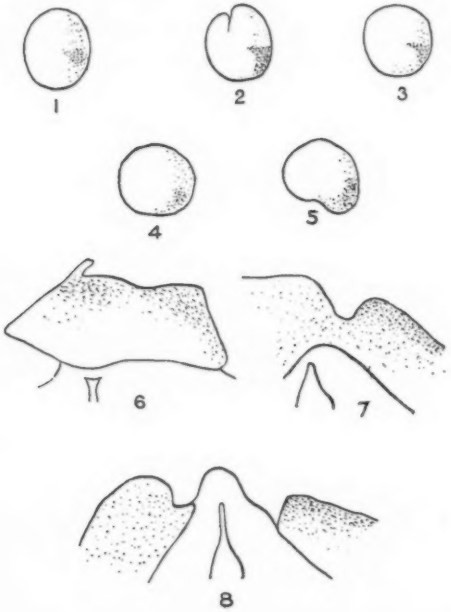
FIG. 2.

FIG. 3.

FIG. 4.

FIG. 5.

towards the centre of the nerve, and the base at the periphery, the whole lying in the upper part of the inferior nasal quadrant. There are scattered degenerated fibres over the whole nasal side, and a few isolated ones upon the temporal side. In sections taken more posteriorly, behind the entrance of the central retinal vessels, the shape of the area occupied by degenerated fibres becomes more crescentic, but is still nasal. Fig. 6 is a nearly vertical (frontal) section of the



chiasma. It shows the fibres crossing, principally in the inferior or ventral part of the chiasma. Fig. 7 is a slightly more oblique section farther back, being in a direction downwards and forwards. The degeneration is therefore ventral and anterior. Fig. 8 is still more oblique, approaching the horizontal, so that only the extreme posterior part of the chiasma is shown, and the tracts are cut more or less

longitudinally. Very few fine dots of degeneration are seen in the chiasma and tract of the same side, the main area of degeneration being in the outer part of the contra-lateral tract. Farther back the fibres spread out over a larger area of the section of the tract, becoming diffuse as they approach their termination.

In sections passing through the bundles of the third nerve as they leave the brain in this monkey, some apparent degeneration was seen on each side. The same occurred to a less extent in the decussation of the fourth nerves. The interpretation of this and other anomalies will be discussed later.

Experiment II.—Jew. Left Eye.

October 30, 1901. A rather larger lesion, about 3 mm. long, was made in a direction tangential to the disc a little in front of the equator in the lower temporal quadrant of the retina. There was practially no hæmorrhage, and the pigmentary degeneration was limited to the lesion.

November 18, 1901. Killed.

The degenerations in the optic nerve are shown in figs. 9 to 11.

Figs. 9, 10, and 11 show that the main area of degeneration is on the temporal side along the whole course of the nerve. It is most marked, and is very dense in the lower temporal quadrant, being more or less wedge-shaped near the eye, and becoming rounder farther back. It tends to become more dorsal near the chiasma, but it is possible that may be due to slight error in orientation. As in I., there is some diffuse generation, most marked on the temporal side. The fibres lie principally in the dorsal part of the chiasma. Many degenerated fibres are seen crossing to the opposite tract. Farther back the fibres lie principally in the central part of the tract of the same side. Posteriorly, they spread out and become more diffuse. In a similar area of the tract of the opposite side, *i.e.*, dorsally and centrally in front, becoming broader behind, there are many finer black spots of degeneration.

The areas including the third and fourth cranial nerves were not sectioned in this brain.

Experiment III.—Bonnet. Left Eye.

November 20, 1901. A very small lesion was made upon the temporal side near the equator, just below the horizontal meridian. There was no bleeding. Macroscopically there was only a white dot at the site of the lesion.

December 7, 1901. Killed.

The degenerations in the optic nerve are shown in figs. 12 to 14.

It will be seen that the degeneration is almost limited to the inferior temporal quadrant, and is very slight. In the chiasma it is at first ventral and anterior in position, gradually tending towards the dorsal surface. In the tract of the same side it is central and dorsal at first, becoming more diffuse posteriorly. There are only a few scattered fibres degenerated in the contra-lateral tract. There was apparent degeneration in the bundles of both third nerves.

Experiment IV.—Rhesus. Right Eye.

January 13, 1902. The lesion was larger, about 3 mm. long, in this retina. It was on the temporal side, a little behind the equator, and extended above and below the horizontal meridian. There was slight hæmorrhage, and, *post mortem*, there was an oval area of pigmentary degeneration, with axes of about 4 mm. by 3·5 mm. The retina was firmly adherent to the choroid over this area.

February 1, 1902. Killed.

Figs. 15 to 17 show the degenerations in the optic nerve.

It is seen to be diffused over the whole temporal side of the nerve, without any special area of concentration. In the chiasma it occupies the central and dorsal parts. There is no degeneration in the ventral part. In the tract of the same side the degeneration is arranged much the same as in II., but more fibres are affected. There is a finer, scattered degeneration in the contra-lateral tract.

The third and fourth nerves were not cut.

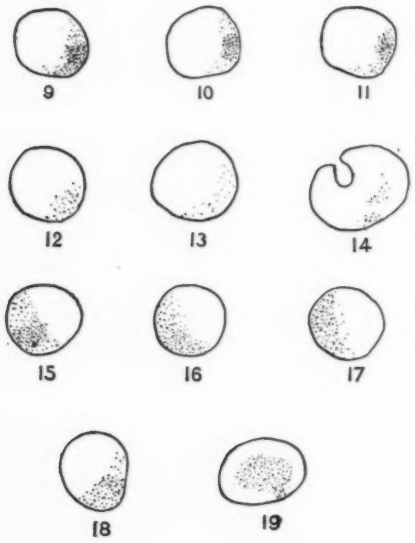
Experiment V.—Rhœsus. Left Eye.

January 14, 1902. A small lesion was made between the macula and the disc, but at a slightly lower level. It was rather

deep, injuring the choroid and sclera, and there was some hæmorrhage.

January 28, 1902. This monkey died in the morning; it was dissected about two hours afterwards.

Fig. 18 shows the distribution of the degeneration in the anterior part of the nerve. Posteriorly it became more central. It occupied the central part of the chiasma, and continued central, and rather dorsal in the anterior part of



the same tract, becoming more diffuse posteriorly. There was a large amount of degeneration considering the small extent of the lesion. This was probably due to its proximity to the disc and its situation in the neighbourhood of the macula. There was fine degeneration in the contra-lateral tract, the fibres crossing in the central part of the chiasma.

There was apparent degeneration in the bundles of both third nerves.

Experiment VI.—Rhæsus. Left Eye.

January 25, 1902. A lesion, 2mm. long, was made in a direction down and out, starting 2mm. down and out from the fovea centralis. There was considerable hæmorrhage into the vitreous.

February 15, 1902. Killed.

Fig. 19 shows the distribution of the degeneration in the posterior part of the nerve.

In the anterior part of the nerve it is most marked on the temporal side, especially just below the horizontal; but there is also a considerable amount of degeneration over the whole area of the section. It is chiefly central in the anterior part of the chiasma; in the posterior part, where the sections are more oblique, *i.e.* about half way between vertical and horizontal, it occupies a crescentic area at the periphery of each side with a connecting band in front. In this situation, therefore, the degeneration tends to become dorsal and external. Farther back, at the commencement of the tracts, there is degeneration in the central, and slightly dorsal parts on each side; and this becomes diffused over the whole tract still more posteriorly.

There is apparent degeneration in the bundles of both third nerves (Plate I., fig. 5).

REMARKS.

(1) *The optic nerve on the side of the lesion.*—My experiments on the monkey agree, upon the whole, with the previous observations of Pick, and of Dean and Usher upon rabbits. They also afford some confirmation of the experiment of Dean and Usher upon a monkey, and of the results arrived at by pathological investigation of cases of toxic amblyopia, in which the papillo-macular bundle is particularly involved. [Samelsohn (5), Nettleship (6), Vossius (7), Uhthoff (8), &c. (9), and especially a very important case reported recently by Birch-Hirschfeld (10).]

Pick's statement, quoted above, holds good as a general conclusion, so far as it refers to the optic nerve. I have invariably found some diffuse degeneration, and this is scarcely to be wondered at. The lesion made by the point

of a Graefe's knife is minimal, probably much less than by the point of a galvano-cautery. At the same time, in dealing with such a delicate structure as the retina, it is not surprising if the injury is not absolutely localised. It is only rarely possible to effect one's purpose without injury of the choroid or even the sclerotic, and it is impossible to entirely avoid the retinal vessels. A slight amount of hæmorrhage into the vitreous usually occurs, and the mere passage of the narrow knife across the eye must lead to reactive changes, probably accompanied by transient shrinking of the vitreous, which may well interfere with the nutrition of ganglion-cells in other parts of the retina.

As might also be expected, the nearer the lesion is to the optic disc, the greater is the resultant degeneration, for not only are the ganglion-cells destroyed, but the axons of ganglion-cells over a large peripheral area are also cut through. The experiments of Baquis and others afford no evidence of regeneration in these fibres, and as they belong strictly to the central nervous system, it is inherently improbable. Moreover, the time allowed is probably too short.

The very definite course of the macular fibres, which do not follow the law which Pick has stated, must cause some dislocation of the other temporal fibres; but the method is not sufficiently accurate to elucidate this point. It may possibly be settled in the future by pathological observations.

One slight modification of the general law as to the localisation of the fibres may be noted, viz., that in the posterior part of the nerve as it approaches the chiasma, the nasal fibres tend towards the ventral side, and the temporal fibres tend towards the dorsal side.

(2) *The optic nerve on the uninjured side.*—Both Pick and Dean and Usher, observed signs of degeneration in the nerve of the opposite—uninjured—side. This observation I am obliged to confirm. It may be mentioned at once that degeneration in my sections was limited to the visual paths, *i.e.*, there was no trace of it in other parts of the brain, actually forming parts of the sections, and therefore subjected to identically the same method of preparation.

PLATE II.

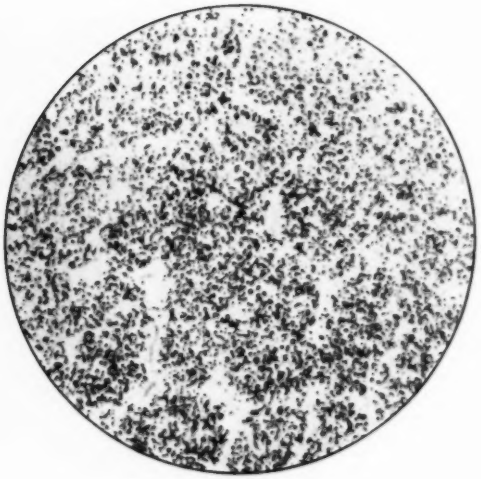


FIG. 1.

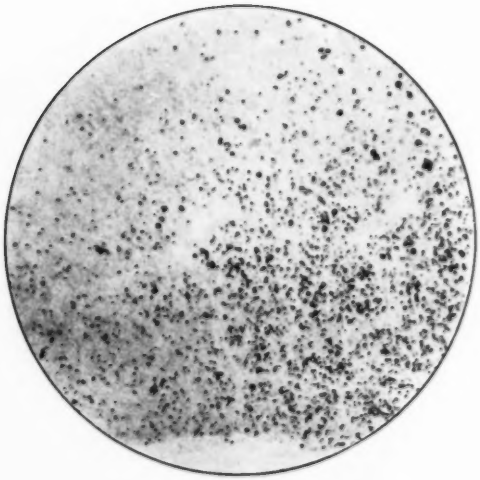


FIG. 2.

In all the specimens it was a diffuse degeneration, usually without very definite areas of concentration, and always considerably less than on the injured side. The degeneration could be traced throughout the length of the nerve, and such concentration of fibres as occurred retained its relative position in all the sections. As a rule this was on the homonymous side of the nerve, as compared with the side of the lesion. Thus in Experiments II., IV., and V., with temporal lesions, the degenerated fibres were principally upon the external sides in both nerves. In Experiment III., with a very small temporal lesion, there were very few degenerated fibres in the other nerve. In Experiment VI. the degeneration was diffuse. In Experiment I. it was also diffuse, but there were a good many degenerated fibres upon the outer side of this nerve, although the lesion was nasal.

I must confess to scepticism when reading of these degenerations in the papers of previous observers, which was only allayed when I found that it was a constant result in my own experiments. One is naturally led to doubt whether it is not due to some error in technique; but the earlier observations were made with the original Marchi method, and in my experiments all the degenerations were limited to visual paths. Professor Schäfer has pointed out the necessity of getting rid of all traces of formol before placing the specimens in the osmic acid mixture, and this I was careful to do by thorough washing in running water. That the appearances are exactly those of degenerations is shown by the illustrations under a high power in Plate II., one of which is taken from the nerve on the side of the lesion, and the other from the opposite nerve.

There is one pathological examination on record which affords some support to this result. Kellermann (11), in a case of old-standing atrophy of the left optic nerve, found a small tract of degeneration in the right nerve, ventro-lateral near the eye, becoming central near the chiasma, and therefore running in the course of the macular bundle. No abnormality of vision was noticed during life, and the central vessels entered the nerve at the inner and lower part (this is not invariable), so that the bundle ran independently of

them. Kellermann attributes the degeneration to compression of the fibres in the chiasma, due to shrinking from atrophy of the fibres of the left nerve. Hebold (12), in a similar case, using Pal's method, found the nerve sound; but the method is not sufficiently sensitive for the purpose. Deutschmann (13), Henschen, and others have also been unable to demonstrate degeneration in pathological cases.

Kellermann's explanation of degeneration in the nerve of the uninjured side is very improbable; there is no evidence in its favour, and much of a general nature against it. Usher and Dean suggest that fat may be removed from the degenerated nerve and carried by lymphatics and deposited in the opposite nerve. This suggestion is equally far-fetched. We are forced to conclude that the degeneration is a genuine one, and, if so, what is the nature of the fibres involved? It is not probable, as Usher and Dean point out, that they are concerned in the pupillary reflexes, as these reflexes remain absolutely unimpaired. We are forced to conclude that they belong to some form of inter-retinal fibres—a reversion, in a sense, to the old inter-retinal tract (commissura arcuata anterior of Hannover, vordere Bogen commissur of Stilling). Ramon y Cajal (14) has demonstrated, by the methylene blue method in rabbits, a division of the optic fibres, and Kölliker discovered an isolated example in a human embryo. Bernheimer (15) was struck by the variety in the size of the fibres in the chiasma, so that it appears in many places as if the larger fibres divided. It is not improbable that the degenerated fibres in the nerve of the uninjured side are collaterals, and that they are distributed to physiologically corresponding parts of the opposite retina, possibly inducing chemical changes in the visual substances or movements in the cells, and so afferent impulses which subserve a modified type of binocular vision. This, however, must be left for further investigation.

(3) *The optic tracts.*—In all cases there was degeneration in both tracts. This may be explained partly by the diffuse injury which probably always results from the lesion, and which is manifested by diffuse degeneration in the nerve. I do not think that this accounts for it entirely. There are

apparently more fibres degenerated in the tracts than in the nerve, and we are here even more powerfully forced to the conclusion that division of the fibres occurs. Most of the experiments were purposely temporal lesions, in order, if possible, to obtain a pure degeneration in the homolateral tract. In these cases the degeneration in the contra-lateral tract usually showed smaller black globules, as if less myelin was present. Probably these were finer fibres—in fact, collaterals.

(4) *Apparent degeneration in third and fourth nerves.*—I do not think that this was a true degeneration, but an artefact similar to that obtained by Marchi in some of his early experiments.

The expenses of this research were defrayed by a grant from the Royal Society.

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NOTE ON THE ARTERIAL SUPPLY OF THE BRAIN IN ANTHROPOID APES.

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AMONG features of human character pertaining to the anthropoid apes we find one not hitherto recorded, namely, the existence in the cerebral arterial supply of a *Circulus Willisii* resembling that of man. In these highest apes, as in man, an interior communicating artery quite frequently completes the *circulus* in front. "In all the lower mammals," Mr. Parsons, who has recently examined the arrangement of the blood-vessels of the brain of a large number of mammalian forms, writes us, "which I have examined, including the Platyrrhine monkeys, *Cercopithecus*, &c., I find no anterior communicating artery." In those lower forms, instead of the pair of large anterior cerebral arteries, there is but a single azygos-vessel, which in its course forward gives on either hand branches to the right and left hemispheres respectively. Apart from Mr. Parsons' morphological work, which has not yet appeared *in extenso*, the only description we know concerning the arterial supply of the brain in the anthropoid apes is furnished by Professor Bolk in his recent monograph on the naked eye features of the brain of the Orang. A detailed account is there given of the arrangement of the arteries at the base in two specimens of Orang brain. He writes[1]: "Die Hauptstämme werden auch hier durch die beiden Carotiden und Arteriæ vertebrales

[1] L. BOLK. "Overdruk uit Petrus Camper Nederlandsche Bijdragen tot de Anat. I., i. II." "Ueber das Gehirn v. Orang-Utan."

dargestellt, welche intracraniell zwar anastomosiren jedoch bei keinem der zwei Exemplaren einen geschlossenen Circulus arteriosus bildeten, da die Arteria communicans anterior in beiden Fällen fehlte."

Our observations have been obtained on six Chimpanzees and on one Orang-outang. Of the specimens classed as Chimpanzees, one was of the variety termed the Koola-kaamba, supposed by some observers to be a cross between *Troglodytes niger* and *Troglodytes gorilla*. The *Circulus arteriosus* found in five of these specimens was of what may be termed the human type. In three Chimpanzees, two large anterior cerebral arteries were united by a short junctional vessel, an *arteria communicans anterior*. In one Chimpanzee the junction between the two anterior cerebral arteries was not effected by a separate vessel coursing from one to the other, but by what amounted to a practical lateral fusion of the two trunks together in the middle line for a short distance, *i.e.*, about 4 millimeters. In the Koola-kaamba the *circulus* was completed by a short but distinct *arteria communicans anterior*. So also in the Orang; our specimen possessed an anterior communicating artery, measuring *post mortem* 7 millimeters in length, and about 1·3 millimeters in diameter, and completing the *circulus* as it is completed in man.[1]

In a sixth specimen of Chimpanzee there was the single azygos anterior cerebral artery such as is found in the lower monkeys and in mammals generally.

A *Circulus arteriosus* of human type thus existing in these anthropoids, it becomes of interest to enquire as to the freedom in them of cross anastomosis in the blood supply of the cerebral hemispheres. This point we have examined in four Chimpanzees.

In none of these animals did occlusion of one common carotid produce either spasm or unmistakable alteration of the excitability to faradism of the motor region of the cerebral cortex. The blood-vessels for their occlusion were laid bare and silk ligatures passed under them. There is

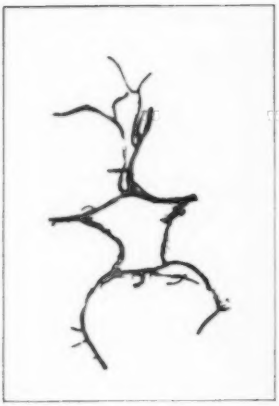
[1] The actual specimens were demonstrated at a meeting of the Liverpool Medical Institution, on February 20th, 1902.

not the least doubt that on each occasion the vessel it was desired to occlude was closed absolutely throughout the whole of the desired period. The occlusion was maintained for eight minutes. In one case during the occlusion the pulsatile movement of the hemisphere where exposed, namely, over the fronto-parietal region, became imperceptible to inspection. But the motor responses to faradic stimulation tested each half minute revealed no obvious alteration.

In two Chimpanzees we found simultaneous occlusion of both carotids fail to evoke any convulsions or to extinguish or markedly diminish the excitability to faradism of the motor region of the cortex, although the complete double occlusion was maintained for eight minutes without any intermission. At the end of the second minute in one of these experiments the response of the leg area to faradisation seemed brisker than before the occlusion of the carotids, but this increase, whatever its origin, quickly subsided and the responses subsequently continued not noticeably different in any way from those obtained at the outset and before the occlusion. The leg-area in this experiment was the region examined by the stimulation, but in the whole of the exposed portion of the brain pulsation, as judged by inspection, was diminished even to extinction under the double carotid occlusion.

In a third Chimpanzee the similar experiment elicited results different to the above. Occlusion of both carotids suppressed the motor response of the cortex in 100 seconds in one hemisphere (right hemisphere) and in 120 seconds in the other hemisphere. The occlusion, it is noteworthy, did not produce convulsions. On releasing the carotids the excitability of the motor area to faradisation reappeared in 75 seconds in the left hemisphere and in about 85 seconds in the opposite.

In a fourth Chimpanzee, namely, that specimen found subsequently to have a *circulus arteriosus* of the ordinary mammalian type, and not resembling the human, occlusion of the right carotid alone produced no obvious alteration in the reply of the arm area of the right hemisphere during a period of five minutes of maintained occlusion. The



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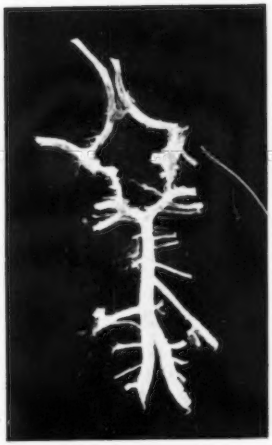

FIG. 2.

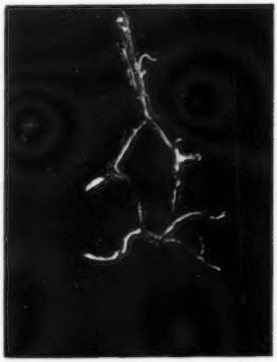

FIG. 3.

Photographs of "Circles of Willis" from Anthropoid Apes.

FIG. 1.—From Chimpanzee.

FIG. 2.—From Orang-Utang.

FIG. 3.—From Chimpanzee, less usual type, the anterior cerebral arteries unite to a common trunk for a distance of four millimetres.

testing was made every half minute. Simultaneous occlusion of both carotids extinguished the reactions from the right hemisphere's arm area in four and a half minutes. The occlusion was maintained for a minute and a half after extinction of faradic excitability. Reactions became once more elicitable ninety seconds after the carotids had been freed.

The above observations establish, therefore, in the first place, that in the Chimpanzee and Orang an arterial circle of Willis of the human type is met with; although, as shown by Bolk's two Orang brains and by one of our Chimpanzees, it is not met with invariably. In the second place, they show that in collateral supply of the brain by anastomotic arterial provision, there is, just as with the morphology of the arterial circle, considerable range of individual variation. In some Chimpanzees the arterial anastomosis is found experimentally to have sufficient freedom for an occlusion of both carotids maintained for eight minutes, to make no obvious alteration in the faradic excitability of the cortex, at least, in its motor region. In other individuals such occlusion is found to rapidly paralyze the cortex, at any rate, in its motor region, when tested by electrical stimulation. This conclusion harmonises strikingly with the conclusion drawn by L. Hill regarding the efficiency of the circle of Willis in man. Hill states:[1] "The efficiency of the anastomosis through the circle of Willis varies in different individuals. Sudden compression of one common carotid artery in some men produces epileptic spasm, and ligation of this artery has been followed in some by more or less temporary paralysis on the opposite side of the body; in others the effect is *nil*."

[1] SCHÄFER'S "Textbook of Physiology," vol. ii., p. 148.

EXPERIMENTS ON THE CONDUCTIVITY OF THE SPINAL CORD RENDERED ANÆMIC BY COMPRESSION OF THE AORTA.

BY MAX LOEWENTHAL, M.D.WÜRZBG., M.R.C.P.LOND.

Historical Record.

Since Nicolas Steno stated in 1667 that occlusion of the aorta is followed by paraplegia, this subject has received the attention of many investigators. This phenomenon, also observed by Haller and Sir Astley Cooper, was considered to be of peripheral origin, until, nearly two centuries after its discovery, Kussmaul and Tenner showed that the "paraplégie ischémique," as it was later named by Jaccoud, is not due to anæmia of muscles and nerves, but to anæmia of the spinal cord. A year afterwards, Sir William Gull published his clinical observation of a case of paraplegia following obstruction of the abdominal aorta within two minutes. Schiffer and Weil and other writers corroborated Kussmaul and Tenner's views. At about the same time Richet and Claude Bernard studied the effect arrest of the circulation has on the reflexes.

The former observed that in the rabbit the reflexes are arrested in less than one minute, the latter, and after him Freusberg, that they persist much longer in mammals, if the animal has previously been cooled for some hours, or if the circulation has been artificially weakened. According to Bernard, the warm-blooded animal loses its spinal excitability quicker than the cold-blooded, the bird quicker than the mammal.

Schiff made a very interesting observation. If the spinal cord of a cat has been severed in the thoracic region and the circulation arrested in the isolated portion of the cord,

powerful contractions of the muscles of the hind limbs and tail ensue. He as well as Richet observed that a high degree of anæmia does not at once abolish, but rather increases, the sensitiveness of the nervous system, and bled dogs in order to heighten their reflex excitability. Richet is the first to make the following important remark with regard to the human subject :—"Abundant hæmorrhages augment the medullary excitability. The greater excitability of the nervous system in chlorotic (patients) coincides with the general anæmia." This appears to be a general law in the animal tissue, for Richet found this initial increase of activity in anæmia also in the peripheral nerves, and instances the painful attacks of Raynaud's disease and the sometimes severe pain following ligation of arteries. The same holds good, according to Faivre, for the nerves and muscles of the frog. Richet also compressed the bulb of the aorta in the rabbit, and found the eye reflex gone after four seconds. If the circulation was interrupted for forty seconds, its re-establishment failed to restore muscular movements and reflexes.

The effects of ischæmia were slower to come in young than in old animals. The above statements as regards an initial increase of activity of the anæmic cord, are supported by Prévost's researches, who, after compression of the abdominal aorta, observed first exaltation and afterwards depression of the knee-jerk. Important contributions to the subject of spinal anæmia were also made by Frédéricq, Colson, Münzer and Wiener, and Brown-Séquard.

The following contributions are of a more recent date. H. E. Hering tried to solve the question, whether it is only the highly vascular gray matter that is responsible for ischæmic paralysis, or whether the white matter has a share in it. He found that simultaneous compression of the carotid and vertebral arteries render the cerebral white matter inexcitable or incapable of conduction, so that cerebral stimulation failed after a certain time to penetrate into the medulla and to evoke the muscular response. From this he concludes that compression of the aorta will likewise deprive the white matter of the cord, especially its long

tracts, of their conductivity, there being no essential difference between the cerebral and medullary white matter, neither as regards their structure nor their vascularity. Unfortunately the article does not give the length of time which elapses from the moment the blood supply has been cut off until the conductivity is destroyed. As long ago as 1881, Minkovski (cited by Hering) made the same experiment, and obtained the same results.

The well-known degeneration succeeding a prolonged compression of the aorta exhibits some peculiarities which, in contrast to Hering's deductions, show a great resistance of the white matter against prolonged anæmia; for, according to Ehrlich and Brieger, Colson, and other writers, there is hardly any degeneration to be found in the posterior roots, dorsal columns, and pyramidal tracts, but especially in those fibres which originate in the central gray matter. The degeneration in these fibres is not a primary one, but a secondary degeneration caused by destruction of the mother cell. The intervertebral ganglion is not easily destroyed, and cannot be considered functionally equivalent to the gray matter. All those fibres which hail from undamaged cells escape, although they have also been exposed to a prolonged lack of nutrition. If these long tracts are not destroyed by an hour's compression of the aorta, it would be very remarkable indeed if the white cerebral substance lost its conductivity in a few minutes. I shall return to this question later. Langendorff has proved by experiment that ischæmic anæsthesia does not originate in the intervertebral ganglion, but in the posterior cornua. Another proof has been given by H. E. Hering, who compressed the aorta in rabbits and found that stimulation of the central stump of the posterior root evokes no reflex movements, nor did he obtain any reflex by dipping the animal's paw into hot water. This shows that the primary interruption of the reflex path must be situated inside the medulla.

Ascher and Arnold performed a series of experiments on the same subject, and found that the different functions of the spinal cord are not destroyed simultaneously,

but in a certain succession. Motility is lost first, whilst the sensory paths still conduct, for at a time when the posterior half of the rabbit is already motionless, stimulation of the crural nerve excites movements of the anterior extremities. After this distant reflex is abolished, there remains as the last visible reflex a slight alteration in the breathing. The very last surviving reflex is a distinct rise of the blood pressure.

When studying the experimental anæmia of the spinal cord, one must strictly distinguish between its excitability and its conductivity for impulses coming from outside the cord. The conductivity may be altered for centripetal and centrifugal impulses. The former, as the historical record shows, has been the subject of much research, but the latter has hitherto, to my knowledge, received no attention.

At the suggestion of Professor Sherrington, I commenced a series of experiments in February, 1899, in order to study the effect which complete anæmia of the spinal cord has on its conductivity for centrifugal impulses, and, besides, repeated some of the experiments performed by others with regard to reflexes.

Method of Experimenting.

The animals experimented upon were cats. Employing the usual method first, I rendered the lower end of the spinal cord anæmic by compressing the abdominal aorta, but soon abandoned this method, as I found that digital compression of the thoracic aorta can be done more exactly and easily, and moreover excludes a larger portion of the spinal cord from the circulation. A convenient way of compressing the thoracic aorta, is to introduce the index finger, after resecting part of the sixth or seventh rib on the left side, into the pleural cavity, and to compress the aorta against the vertebral column between the index finger and the thumb of the same hand placed outside.

As deficient aëration of the blood owing to collapse of one lung might mar the value of the results, I deemed it advis-

able to keep up artificial respiration. For this purpose tracheotomy was performed, and the stem of a T-shaped glass cannula tied into the trachea. One of the cross branches of the cannula was partly closed with wax to regulate the amount of air passing through the lungs, whilst the second branch was connected by rubber tubing with an automatic air pump worked by a dynamo. In the course of this rubber tube, I inserted a Wolff's bottle for the administration of an anæsthetic, which was either an ether-chloroform mixture or pure ether.

I first endeavoured to determine the length of time during which the spinal cord retains its conductivity for a stimulus arising from the cerebral cortex, from the moment the blood supply is cut off. To this end, the left motor area of the brain was laid bare by removing the piece of skull covering the left crucial sulcus with trephine and bone forceps and carefully opening the dura mater.

Experimental Observations.

(*A*) *Cortical Stimulation.*

In the first animal experimented upon, a fit commencing in the posterior extremities, was produced on stimulating the hind limb area of the cortex by a faradic current just strong enough to give a response. The aorta was then compressed for two minutes, and the current applied to the same area again. The hind limbs gave no response now, their muscles being atonic and flabby, whilst the fore limbs showed the usual clonic movements.

In the second experiment, the aorta was again compressed, and after two minutes the cortex stimulated, when the fore limbs responded vigorously, and the hind limbs remained motionless and flaccid. On releasing the aorta, the right hind limb was suddenly and spontaneously drawn up for a few seconds. After an interval of ten minutes, the aorta was compressed at the same moment in which excitation of the cortex was commenced, the latter being stimulated for a few seconds at intervals of about ten seconds. At first

the hind limbs responded distinctly more vigorously and promptly than before compression, and with quickly increasing strength, until after about forty seconds the movements began to be weaker, and finally ceased after about sixty seconds. The preponderance of the movements of the hind limbs at the commencement and of those of the fore limbs towards the end of this minute was very distinct. On releasing the aorta after a minute's compression, both hind limbs were immediately drawn up, but this flexor spasm only lasted a moment. This phenomenon I could often observe, if the compression had not lasted much longer than a minute. Repetitions of this experiment in the same animal gave similar results with the difference that the hind limbs became paralysed sooner at every following trial. Similiar results were also obtained in several experiments performed on other animals under the same conditions. After a time averaging eighty seconds, the hind limbs remained motionless. I could always notice an increase in the strength and readiness of the response during the first half, and a decrease, especially quick towards the end, in the second half of the time, during which movements could be obtained. The time which elapses before a response can again be obtained in the hind limbs after re-establishing the circulation, greatly depends on the length of time during which the circulation was interrupted. After two or three minutes the cord has regained its conductivity, unless the anæmia has lasted too long.

(*B*) *Spinal Fits.*

Three or four times, I could observe a peculiar phenomenon in different animals. At the time when ischæmic paralysis was commencing, the hair of the tail became erect and immediately afterwards a powerful extension tonus with slow writhing movements of small range seized the posterior half of the animal's body. There was flexion of spine and hips and extension of tail, knees, and ankles. I was struck with the likeness between these localised convulsions and those agonal general convulsions one observes in animals bled to death or asphyxiated, and am therefore tempted to

describe these movements as localized or partial agonal convulsions. The contractions of muscles observed by Schiff after section of the cord are probably identical with those observed by myself. Section of the cord may facilitate the occurrence of this phenomenon, but is not essential. These convulsions could several times be brought on by stroking the tail after conduction from the cerebral cortex was abolished. They certainly originate in the gray matter of the spinal cord and therefore deserve the name of "Spinal Fits." Probably the whole of the motor portion of the gray nervous matter is capable of violent explosive discharges, and every accumulation of motor cells throughout the brain and medulla can act as a "cramp-centre." Cortical discharges are of the well-known clonic type and those of the spinal cord chiefly tonic, whilst discharges of the bulbo-pontine gray matter (Kussmaul and Tenner's "cramp-centre") are a mixture of tonic and irregularly clonic, jerky movements. Thus Hughlings Jackson's different levels are represented by different kinds of discharges.

(*C*) *Knee-jerks.*

Four experiments were made in order to study the knee-jerks after compression of the aorta, and it was found that they present the same peculiarity as the cortical response. Instead of gradually becoming weaker from the commencement, the knee-jerk on the contrary shows a rapid increase, until after about half a minute the slightest tap, almost a touch, on the patellar tendon elicits a vigorous jerk. It then gradually lessens and quickly subsides altogether after about eighty seconds. Its re-appearance takes about the same time as that of the cortical response from the time the circulation has been restored.

(*D*) *Peripheral nerves and posterior roots.*

When stimulating the sciatic nerve after compression of the aorta, I could get no reflex movements after from two to three minutes. These movements not being so obvious as the knee-jerk in an anæsthetised animal, it is difficult to state the exact moment when they have ceased, but they

last distinctly longer than the knee-jerk. I could not make out an initial increase such as I observed in the knee-jerk and on cerebral stimulation. Dipping the animal's hind paw into hot water, I could twice observe movements of the fore limbs and forced breathing at a time when the hind limbs were completely motionless. Stimulation of the posterior roots is apt to lead to fallacies, as it is very difficult to be certain that the current is not straying into the cord. On applying a very weak current to the posterior roots at the lumbar enlargement, movements were obtained if the electrodes came too near the cord, but no movement could be elicited at a greater distance unless the strength of current was increased. The same weak current which just gave the response before compression of the aorta, failed to do so after two minutes compression. I was struck with the great irritability of the anæmic spinal cord, and with the length of time it lasted. It even seemed to me that for a long time it is even more irritable than normally. The weakest current applied as late as fifteen minutes after death at the insertion of the posterior roots gave a violent response. Personal observation leaves me no doubt that this is a real reflex carried from the points of entrance of the sensory roots to the motor cells and that it is not due to the anterior roots being stimulated by stray loops of current. If the ventral aspect of the cord is stimulated, the muscles of the same side contract steadily, but if the current affects the vicinity of the posterior roots, the muscles respond also on the other side, and in a jerky manner, giving a series of contractions quickly following each other and greatly resembling the pain reflex.

Remarks.

The first conclusion that can safely be drawn from my own and from other experimenters' results, is the fact that after about two minutes of complete ischæmia no stimuli entering the ischæmic part of the medulla can penetrate into the motor nerve. My experiments prove that stimuli coming from the cerebral cortex do not form an exception

to this rule. The question which remains to be solved concerns the nature and the place of this obstruction to the flow of the nerve current. If Hering's view is correct, the white substance loses its conducting power as well as the gray, and no energy can enter the anæmic part of the cord. It is, however, extremely unlikely that the fibres of the white columns should be deprived of their conductivity in so short a time, as I have already pointed out before. There are several facts opposed to this view. The peripheral nerves, retaining their conductivity for a very long time, resemble the fibres of the central nervous system, from which they only or chiefly differ in their possession of Schwann's sheath, anatomically and functionally, and we should therefore expect a similar power of resistance to a lack of nutrition in both. We know that in prolonged anæmia those fibres which are derived from undamaged cells escape degeneration, though they have been without their blood supply as long as an hour. Why, then, should we believe that they lose their conducting power within a few minutes?

The vascularisation of the white cerebral and medullary substance, moreover, is so scanty that it cannot be greatly dependent on a liberal supply of blood, but it seems to me, apart from these considerations, that Hering's and Minkovski's experiment, however interesting it may be, is not conclusive. It certainly proves that compression of the arteries supplying the brain prevents a stimulus arising from the corona radiata from reaching the motor cells of the anterior horn, but it does not prove that the white substance, in our case the portion of the pyramidal tract coursing through the anæmic area, has been deprived of its conductivity. The main motor path in the lower animals cannot go through the pyramids, for their section in front of the medulla oblongata does not appreciably affect the animal's movements. This being so, it must be proved first that their stimulation under proper precautions can evoke muscular action in the lower animals. The main motor path traverses a complex mechanism containing gray matter, and would, on account of the latter, be interrupted

by compression of the cerebral arteries. Another point to be considered is the depression, or even suppression, first observed by Landois, of cardiac action and respiration caused by ligaturing all the cerebral arteries. This in its turn may depress the activity of the medullary gray matter and act similarly to compression of the aorta. It is my opinion that we must seek the place of interruption in the gray matter, at the points of transit from one neuron to the other.

We do not know how long after anæmia is established the gray matter remains excitable. The fact that stimulation by a very weak current of the tip of the posterior horn excites bilateral muscular movements, may be due to "Stromschleifen." According to Schäfer's "Text-Book of Anatomy," some of the fibres of the anterior roots take their origin in cells of the posterior horn; others go from the anterior horn through the white commissure and leave the cord in the motor roots of the opposite side. This commissure being in the lumbar region situated in the centre of the cord, it is possible for loops of the current straying from the electrodes to reach it, thereby causing bilateral movements. The resulting muscular response, however, resembles that of the pain reflex very closely, and gives one the impression that the stimulus is conducted by the gray substance of the posterior horn to the motor cells. This reaction begins to fade after the lapse of about fifteen minutes.

The remarkable experiments performed by Hoche on the human subject add weight to the latter view. He obtained permission to study the functions of the spinal cord in several decapitated criminals immediately after the execution, and managed to commence his experiments as early as two minutes after the head was severed from the body. He found that no movements of the legs could be obtained by applying the electrodes to the pyramidal tracts exposed in the cut surface, nor could the patellar reflex be obtained. Stimulation of the ventral half of the cord with a minimal current and electrodes 1 mm. apart gave movements in the shoulder and elbow joints of the same side, whilst stimu-

lation of the posterior root was followed by bilateral, exactly symmetrical movements of a different character, crossing of the arms before the chest. Although it is possible that Hoche employed too strong a current, and, consequently, stimulated not only the posterior roots, but also the adjoining parts of the cord, his experiments render the existence of an intimate connection between the sensory and motor gray matter, not quickly severed by death, highly probable.

Conclusions.

(1) The first effect of arrest of the circulation on the functions of the spinal cord is an increase in the readiness and strength of interneural transmission of nerve energy lasting about thirty seconds.

(2) After from one to two minutes, stimuli approaching the gray matter through peripheral nerves or the fibres of the white substance, are not transmitted to the lower motor neuron.

(3) It is probable that every single neuron as a functional unit retains its vitality for a period exceeding fifteen minutes, but that the mechanism which links the separate neurons together is quickly destroyed by death.

(4) The existence of genuine spinal fits cannot be disputed.

The experiments described in this paper were performed in the Physiological Department of the Thompson-Yates Laboratories. My sincerest thanks are due to Professor Sherrington for much valuable advice and help, and to Dr. Hope-Simpson, who devoted much of his time to this research, for his able assistance.

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FURTHER OBSERVATIONS ON A CASE OF CONVULSIONS (TRUNK FIT OR LOWEST LEVEL FIT ?).

BY J. HUGHLINGS JACKSON, M.D., F.R.S.

AND

STANLEY BARNES, M.D., M.R.C.P.

PART I.[1]

THIS is a further report of a case published (BRAIN, Spring No., 1902, part 97), by Dr. Douglas Singer and myself. Although it is convenient, following custom, to use the term *status epilepticus*, the important question, as we then said, is not whether the fits the patients had are to be called epileptic or not. The really important question is, to reproduce part of what we wrote (*op. cit.*), "Where is the lesion (discharge-lesion) which, on its occasional 'intense' discharge, produces a convulsion *beginning* in muscles of the trunk (that is, in muscles of two sides of the body, the normal action of which may be, and often is, bilateral) and *beginning* in those muscles of the two sides of the body simultaneously?" It will be seen that in the "first period" of the *status* Dr. Stanley Barnes describes, the convulsion did not affect the extremities in the slightest degree. In the "second period" the limbs were affected, but after the trunk; Dr. Barnes carefully describes a "march" of the spasm *down* the arms. As ought always to be done, he distinguishes between movements proper, in two attacks of the first period, and spasm (contention of many movements). I think now, considering especially the observations Dr. Stanley Barnes made on the "inspiratory cry" in a certain part of the march of some of the patient's

[1] The first part is by J. H. J., the second by S. B.

attacks, that her fits are probably Lowest Level (Ponto-Bulbar) Fits and not fits of ordinary Epilepsy (Higher Level Fits).

I draw particular attention to Dr. Barnes' observations on the reflexes in and after the fits; these observations seem to me worthy of great attention. It is very striking that the knee-jerks were lost *in* attacks when there was not the least spasm of any limb.

Part II.

History.

The patient, J.K., is the eldest of a family of nine children, all of whom are alive. Most of the other children are said to have a "narrow bridge" to the nose, but no history of any other sign of syphilitic taint can be obtained.

The patient has always had a squint, and in childhood suffered from measles, whooping cough, and scarlet fever. For about two years during the first dentition she suffered from "teething convulsions."

The present illness began at the age of 9 years; the fits at first occured about once a month and gradually increased in frequency. After the age of puberty, their number rapidly increased to several daily. In March, 1901, she was in *status epilepticus* for ten days, followed by a period of complete cessation for a month; the fits then recurred, and in December, 1901, she again passed into *status epilepticus* for sixteen days. At this time she was admitted to the National Hospital, and many of the fits were observed (*vide* Brain, Spring, 1902, "Observations of a case of Convulsions" by Dr. Hughlings Jackson and Dr. Douglas Singer). She remained in hospital for three months longer, and during this time only had one slight attack. The patient then went to the Convalescent Home at Finchley, where she remained for nearly two months, a few slight seizures occurring there. During the second week after her return to her own home a few severe attacks came on, and these continued to occur and increase in number until the fifth week, when for the third time she passed into *status epilepticus*, and was re-admitted to the National Hospital on June 13, 1902.

General Examination.

As in the previous attack of *status epilepticus*, the general examination was deferred until consciousness was regained on

June 27. No material change in her general condition had occurred since her previous admission in December, 1901, so that it is unnecessary to repeat here the description given in the previous paper (*vide* BRAIN, Spring, 1902, p. 125).

The Fits.

The first ten days after admission some 200 fits a day were seen to occur; it is highly probable that the actual number was even larger. The maximum recorded was on the second day, when 394 were observed. After the tenth day the number rapidly diminished, and on the fifteenth day no fit occured. From that day (June 27) until September 2 only one severe and three slight attacks occurred at irregular intervals.

In describing the attacks it will be convenient to classify them as in the previous paper, according as they occurred in the earlier or the later stages of the *status epilepticus*.

Fits occurring in the First Period.

The attacks occurred at intervals of about three minutes, each attack lasting about forty seconds. She was unconscious between the attacks.

Before the attacks, the patient was lying on her back in bed with her head resting on a pillow, the arms lying, as a rule, in front of her. The breathing was quiet and regular, both chest and abdomen moving about normally for a girl of her age; the accessory muscles of respiration were not in action during inspiration.

In every instance in which the onset was particularly watched, a bilateral deepening of respiration with action of the sternomastoids and scaleni was the first sign of an approaching fit. These accessory muscles of respiration did not at once go off into tonic spasm, but contracted in inspiration and relaxed in expiration; after two such inspirations, in the second of which the contraction was more marked than in the first, the sternomastoids and scaleni failed to relax completely in expiration, so that the chest remained unusually expanded although respiration continued for several seconds afterwards.

The contraction of the accessory muscles of respiration appeared to be equal on both sides; it was not very powerful, and the head was never lifted off the pillow; at times a slight rotation of the head occurred, sometimes to the left, occasionally to the right.

Usually at the end of the second inspiration mentioned above, the next movement occurred; this was a contraction of the frontales and levatores palpebrarum of both sides symmetrically. The eyes then turned jerkily to the left, the elevators of the eyebrows and eyelids being at this time in tonic spasm.

The lower segment of the face was next affected, both sides at the same time, but, as a rule, the left side slightly more than the right; the angles of the mouth were drawn downwards and the lips separated. Tonic spasm here rapidly gave way to clonic spasm, but before the latter was fully established the jaws were separated by a tonic spasm of the depressors of the mandible overcoming the contracting masseters and temporals. The teeth, as a rule, were separated about half an inch, and the jaw always opened strictly in the middle line.

Up to this point respiration had continued at the usual rate, although the scaleni and sternomastoids were contracted apparently as much in expiration as in inspiration. Just as the jaw opened, the chest being full, respiration ceased, but not all respiratory movement. The abdomen swelled slowly forwards (diaphragmatic action), and at the same time the chest slowly sank in and diminished in volume, no air either entering or emerging from the glottis. This complex movement continued for about twelve seconds, and then ensued a long-drawn crescendo inspiratory cry; at the beginning of this cry the pitch was high, and gave the impression of air entering the chest through a very narrow glottis owing to great inspiratory effort; later the spasm of the glottis appeared to give way and allow air to enter more and more freely. The cry lasted about five seconds, and as it occurred the abdomen remained fixed in its inspiratory position whilst the chest again filled out. After the cry the respiration was resumed almost at once, and, as usual in her sex, was of the costal type. The eyes before the cry were turned to the left; after it, as they slowly returned to their usual position, the conjunctivæ became suffused and much lachrymation occurred, the tears usually rolling down both cheeks just at the end of the fit.

In the majority of the fits very little cyanosis occurred; in one that was carefully observed there was very marked blueness just before the cry. No noticeable sweating occurred.

In none of the fits did the slightest spasmodic hand or arm movement occur. In two of them, just as the fit was beginning, an irregular purposive-seeming movement was going on in the right upper extremity, the elbow being flexed and the forearm

pronated as though she were going to rub her eyes—a thing she often does between the attacks. There was no spasm about the movement, and it was of an absolutely different nature from the face and neck movement; it never occurred whilst the fit was in progress after the corneal reflex was lost. Apart from this movement, not a trace of muscular contraction occurred in the upper extremities, which were loose and slack at all their joints. The lower extremities were also carefully observed repeatedly, but no movement or muscle contraction could be felt here.

During the attacks the patient was quite unconscious, and she often micturated in or after them. The reflexes were carefully observed in many of the attacks, and deserve mention in some detail.

State of Reflexes in the Fits.

The *corneal reflexes* were only lost at the height of the fit; they began to diminish as soon as the elevation of the eyebrows occurred, and were lost at the time when the jaws were separated. They returned before the face had ceased to twitch, and quickly reached their normal intensity.

The *supra-orbital* reflexes disappeared during the attacks, during, speaking roughly, the same period as the corneal reflexes.

The *jaw-jerk* between the attacks was unusually brisk; it remained so during the attacks, except when the jaw was fixed by spasm of the mandibular muscles.

The *knee-jerks* were carefully and repeatedly tested during several attacks. The method adopted was to support the thigh so that the leg hung down at an angle of about 120°, and the ligamentum patellæ was then tapped with a percussion hammer about once a second, beginning before the commencement of the fit and ending after the end of the fit. Each knee-jerk was tested in several fits. Between the attacks the knee-jerks were brisk, and no alteration occurred at the beginning of a fit until the lower part of the face went into spasm, and breathing had ceased; at this stage the knee-jerk rather suddenly completely disappeared, and remained absent until the cry occurred; it now at once began to return, and just at the end of the fit was more brisk than usual, resuming its usual slightly brisk condition a few seconds later. This observation was confirmed by Dr. Hughlings Jackson and by Dr. Risien Russell on separate occasions. At the risk of appearing tautological, I would reiterate that in these attacks in which the knee-jerks were lost not the least movement or spasm of any limb occurred.

Fits of the Second Period.

On June 22, for the first time, fits were observed in which limb movements occurred. On this day these fits to a large extent alternated with those previously described as "fits of the first period," and in which no limb movement occurred. It was noticeable that the fits in which limb movement occurred were of longer duration and apparently of greater severity than those in which no such limb spasm was present. Repeated and careful observation convinced me that the fits of the two periods began in exactly the same way, the difference being that during the second period, in many instances, the fit spread from the trunk to the limb muscles, so that in the most severe attacks the spasm became general.

The first limb movement to occur was always at the proximal end of one of the upper extremities; usually the left, sometimes the right shoulder group was first affected, the point of the shoulders being shrugged upwards, the arm elevated forwards, then the elbow was flexed, the wrist extended, and the fingers were strongly flexed over the thumb, which was adducted into the palm; in this way the fit could be observed to spread from the proximal to the peripheral terminal muscle groups. The movements were at first tonic and afterwards clonic.

In the lower extremities the extensors of the knee appeared to be first affected; beyond this I was unable to trace the order of involvement of muscle groups, as only two fits were observed in which the legs went into spasm. When in full spasm, however, the legs were, in these two attacks, in the fully extended position, *i.e.*, with extension at hip, knee and ankle. The first lower extremity movement appeared to begin a little later than the first upper extremity movement, but before the whole upper limb was involved. I cannot say whether the left or right leg was the more frequently affected.

None of the above-described limb movements ever occurred until after the "cry" (*vide* "Fits of the First Period").

Slighter Fits.

Beyond the two kinds of fits already described, many slighter attacks were frequently occurring during both periods. In their onset these fits exactly resembled those described as "fits of the first period," but instead of going on until the jaw was depressed, they died away as soon as the upper part of the face had become involved; there was no cry with these attacks. Every gradation

was observed between these slighter attacks and the more severe ones in which the limbs were fully involved.

Mental Condition.

Until June 27, the day on which the fits ceased, no reply in answer to a question could be got from the patient; nor did she utter any sound which would lead one to suppose that she was at all conscious. On that day she first began to speak, but it was evident that she was only dimly conscious, and her ideas appeared to be much distorted. At times also she appeared to be suffering from hallucinations of vision and hearing. By June 28 she could reply sensibly to very simple questions, and thereafter she gradually resumed her usual mental state, so that by July 18 she could write letters passably well.

Incontinence of urine and fæces continued for nearly a week after all fits had ceased, but is now (September 8) no longer troublesome.

HEREDITARY APHASIA: A FAMILY DISEASE OF THE CENTRAL NERVOUS SYSTEM, DUE POSSIBLY TO CONGENITAL SYPHILIS.

BY WILLIAM GREAM STONE, M.A., M.D.OXON., F.R.C.S.

AND

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I.

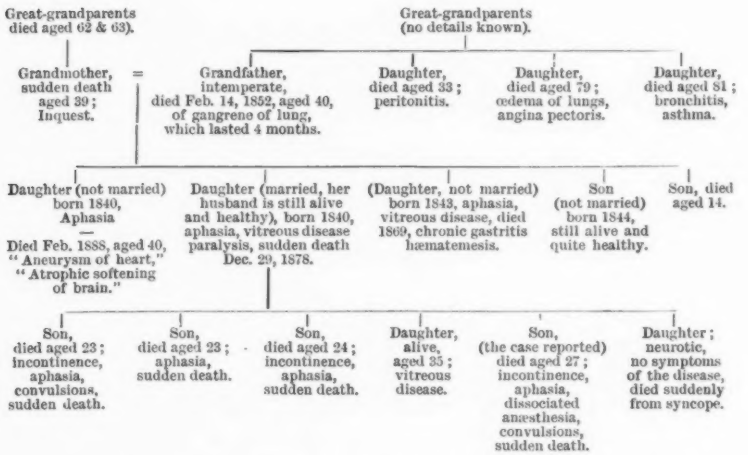
UNDER the title of Hereditary Aphasia we have attempted to describe a disease that has been observed in eight members of a family; three cases occurring in one generation, and five in the generation following. There is a sufficiently close resemblance between each one of the series of cases and the rest to exclude the notion of an accidental similarity, and to justify the conclusion that we have to deal with one disease in all the cases, a disease due to the same cause throughout, and capable of recognition if it recurs by a limited group of well defined symptoms. The morbid anatomy and histology have been worked out in the latest of the cases, and the lesions observed suggest, though far from conclusively, a syphilitic origin for the disease. If this point can be proved, it will be of special interest, for the taint of the disease will have reached the grandchildren of the person originally affected.

The main features of the disease, which does not become manifest until the patient is attaining to adult life, are the following:—Incontinence of urine,[1] attacks of temporary aphasia with loss of power on the right side of the body, gradually increasing opacities in the vitreous humor of the eyes, loss or diminution of the senses by which pain and

[1] The term incontinence is here used, as the affection was so described in the earlier cases; but the symptom would be more correctly described as "retention of urine."

temperature are appreciated, muscular weakness, epileptiform convulsions, and sudden death preceded by complete unconsciousness. Wasting of the soft tissues is marked only during the later stages of the disease.

A family tree will briefly show the number of children in each generation, and how they were affected by the disease:—


Great-grandparents died aged 62 & 63).
Great-grandparents (no details known).
Grandmother, sudden death aged 39; Inquest.
=
Grandfather, intemperate, died Feb. 14, 1852, aged 40, of gangrene of lung, which lasted 4 months.
Daughter, died aged 33; peritonitis.
Daughter, died aged 79; œdema of lungs, angina pectoris.
Daughter, died aged 81; bronchitis, asthma.
Daughter (not married) born 1840, Aphasia — Died Feb. 1888, aged 40, "Aneurysm of heart," "Atrophic softening of brain."
Daughter (married, her husband is still alive and healthy), born 1840, aphasia, vitreous disease paralysis, sudden death Dec. 29, 1878.
(Daughter, not married) born 1843, aphasia, vitreous disease, died 1869, chronic gastritis hæmatemesis.
Son (not married) born 1844, still alive and quite healthy.
Son, died aged 14.
Son, died aged 23; incontinence, aphasia, convulsions, sudden death.
Son, died aged 23; aphasia, sudden death.
Son, died aged 24; incontinence, aphasia, sudden death.
Daughter, alive, aged 35; vitreous disease.
Son, (the case reported) died aged 27; incontinence, aphasia, dissociated anæsthesia, convulsions, sudden death.
Daughter; neurotic, no symptoms of the disease, died suddenly from syncope.

It will be seen from this that there is no evidence of the disease in the great-grandparents on either side. Of the maternal grandparents, both furnish some suspicious points. The grandmother died suddenly, so suddenly as to require an inquest. The coroner's verdict, however, gives no details, only stating that "she died naturally and not from any "violence." The grandfather led an intemperate life, and died in the London Hospital when 40 years old of "gangrene of the lung." This was a chronic illness, lasting four months, but unfortunately no *post-mortem* examination was made, and no record of the case has been preserved to show whether the disease was syphilitic or not.

Of the second generation one male is now alive, and healthy, at the age of 67. He was younger than his three sisters. The only other male child died in his fifteenth

year, presumably too early to show symptoms of the disease. The three daughters all suffered from it. The mother of our patient was healthy as a girl and while a young woman. The only abnormal fact that is related of her previous to her marriage is that she suffered from time to time from a "curious reddish eruption on the finger-tips." She was married at 27, and shortly afterwards began to suffer from attacks of aphasia, which came on at long intervals, "perhaps two or three times in the year." On these occasions she also "used to drop things." Seven years after her marriage, at the age of 34, her sight had become so much affected that she only retained a weak perception of light. Whether she suffered from urinary troubles cannot now be ascertained. She died at the age of 38, after four years' partial paralysis, the latter appearing to have taken the place of the occasional attacks at about the same time that the amblyopia became extreme. Her death occurred on December 29, 1878, and was ascribed to apoplexy.

Of her two sisters, the elder died on February 6, 1880, aged 40. Death was ascribed to an "aneurism of the heart," supervening upon "atrophic softening of the brain"; the latter had been of several years' duration. It is remembered of her that she had temporary attacks of aphasia, with loss of power in the right arm. She had no epileptiform attack, or at all events, none that caused unconsciousness. She does not seem to have suffered from any ocular trouble, and there is no evidence of "incontinence of urine."

The younger sister died July 14, 1869, aged 26. Her death was due to hæmorrhage from a gastric ulcer. She suffered from temporary attacks of aphasia and paralysis in the right arm; and also, like her married sister, from a gradual loss of vision. The following account of the eye symptoms in both of his patients has kindly been furnished to us by Mr. Brudenell Carter, whom they consulted twenty-seven years ago; it is especially interesting in conjunction with Mr. Lawford's report on our patient, which is given later. "(The married sister) had slight deep-seated cloudiness of the vitreous, when seen in 1875, with slight

impairment of vision; the right eye to about a $\frac{1}{2}$, the left to about $\frac{2}{3}$ of normal vision. Partly from the nature of the case and partly from the treatment by hyd. perchlor. and pot. iod., I have little doubt that I regarded the case as specific, but my notes do not say so. My last record is that the vision remained stationary, after slight improvement." This note was made three years before the patient's death, and, as has already been mentioned, blindness became almost complete before the end. Of the other sister Mr. Brudenell Carter writes: "I saw her on December 10, 1874, and on January 3, February 1, and March 23, 1875. My first note is, "Turbidity of R. vitreous, commencing ditto in L., probably hæmorrhagic in origin. Neurotic tendencies; occasional speechlessness with temporary paralysis of right arm. Under treatment the vision of R. rose from $\frac{8}{50}$ to $\frac{8}{25}$; the urine was normal."

We now come to the generation of the patient with whose case the present writers have been acquainted. There were six children, four sons and two daughters. The three elder sons died between the ages of 22 and 24. Of the two daughters one was older, one younger, than our patient. The elder of the two was healthy till her 30th year, but since then her eyesight has become defective, and the nature of the defect proves in this case also to consist in vitreous opacities. She is not known to have had any other symptoms of the disease. The younger daughter was neurotic, but showed none of the special symptoms characteristic of the disease. She died suddenly at the age of 24, from sudden heart failure during a severe attack of diarrhœa. There was no *post-mortem* examination.

The eldest son died at the age of 23, death being ascribed to "apoplexy." The first symptom of disease in his case is said to have been incontinence[1] of urine, which commenced in his twenty-second year. Previous to that time he had enjoyed good health, being educated at a public school where he played cricket and other games. After leaving school he

[1] Probably really retention.

"crammed" hard for the army. The "incontinence," at first intermittent, gradually became established; it was presently followed by attacks of aphasia, short in duration. Later on he had several epileptiform seizures, falling in the street and elsewhere; he never hurt himself seriously by these falls, but he became quite unconscious, and the tongue was bitten. He was not drowsy after the attacks. It is also reported that he occasionally became unconscious for a few minutes without other symptoms.

The second son was healthy as a boy, but did not go in for any form of athletics. He reached the age of 22 without misadventure; but then, one morning at breakfast, he suddenly lost the use of his right hand, while trying to lift the cover off a dish. The weakness lasted for two or three hours. There is some doubt as to whether aphasia was also observed at this time; but later on he did have one or two attacks of aphasia, and it was decided to send him for a long voyage to Australia on account of his "want of tone." He improved during the early part of the voyage; but one day, in rough weather, he was found insensible in his cabin, and he died without recovering consciousness. He does not seem to have suffered at any time from urinary troubles.

The third brother was also healthy for the first 22 years of his life. He played cricket and football at school, and went into his father's office when he grew up. He died at the age of 24, having been ill two years. He had suffered from "incontinence" for about twelve months before his death. He also suffered from attacks of temporary aphasia, and those who were with him related that the lips became full and the face congested before an attack. He suffered greatly from constipation, sometimes passing no motion for a week; he gradually grew weaker, heavier, and more drowsy; finally he became suddenly unconscious, and died. Towards the end, when very weak, he passed fæces as well as urine unconsciously.

The fourth son was the only one known to us, who saw him first in December, 1897. He was then 23 years of age, and had begun to show symptoms of the disease about nine months previously. His appearance was that of a strongly

built, rather tall young man. He had been healthy during boyhood and fond of all forms of athletics, including gymnastics, cricket and football. He had not suffered from incontinence as a child. There is no record of illnesses in childhood, except some unnamed illness at about the age of 14, a bilious attack followed by fever and delirium. At times he had been given to sleep-walking. As recently as 1895, when 20 or 21 years of age, he had been able to walk thirty-two miles in a day without more than ordinary fatigue.

In his case also the earliest symptom observed had been "incontinence of urine"; though an unusual degree of constipation had been present for two years before this occurred. It was preceded by pain in the tip of the penis, sufficiently severe to make him consult a doctor: the first escape of urine followed a week later. Since that time it had occurred only during the night; but, with three exceptions, it had occurred every night from March to December. The sexual functions seem to have been disturbed at the same time, the patient losing all sexual desire, and never having an erection of the penis. The account given by him in December, 1897, suggested overflow from a distended and atonic bladder rather than true incontinence. He said that, when he had passed water, more came on further effort; and that "coughing would then again cause the stream to flow out in jerks." The stream was at all times weak, and he passed water for about a quarter of an hour before going to bed, doing so while kneeling to say his prayers. It was at eight o'clock in the evening that he first came for advice, and a catheter was then passed. No stricture or other obstruction was found. A pint of urine was drawn off; it came fairly strongly at first, but for a long while at the end it merely trickled. The urine was acid, it contained albumen and pus, no casts were found. The albumen and pus disappeared later when the bladder had for some time been regularly emptied by the catheter and washed out at intervals.

Of other symptoms, the only one noticed at this time was some defect of vision. It caused him no serious in-

convenience; but he noticed that there were spots in groups, before the right eye. The pupils were at this time normal in size and shape, and re-acted both to light accommodation. The muscular strength was good everywhere. Knee-jerks were present, but perhaps a trifle sluggish. He had occasionally sudden and brief pains in the legs. The tongue was rather red and had a swollen appearance.

After this he was not seen for two months, re-appearing in February, 1898. The "incontinence" had become less troublesome, but there was again pus and albumen in the urine, and he did not seem to know by his sensations when the bladder was over-distended. He went away for several months to the Riviera, and was next seen in November, 1898, after an interval of nine months. He was suffering at the time from a febrile attack, with temperature 101-102° F., the fever lasting for four days. He had no headache, did not complain of pain in his back or limbs, was listless and heavy, and inclined to wander in his talk. On recovering, he gave some account of his experiences during the preceding nine months, and a fuller examination was made of the nervous system. He said that he had been better during the summer, but thought that he had lost some strength. He had come to use the catheter regularly, and could not pass water without it. The pus and albumen were no longer present, there was some slight improvement in the force with which the urine was expelled through the catheter.

Examination revealed the following facts:—

(1) In common sensation there was nowhere any change from the normal.

(2) The sense of pain and the temperature-sense were very markedly affected. While in bed he had allowed both his feet to remain in contact with an uncovered hot-water bottle; and while he felt no pain, large burns had resulted. These healed slowly but satisfactorily. The accompanying diagram shows fairly accurately the degree of analgesia, and the regions affected. It was most marked over both legs below the knee. On the right leg in front, it ascended also

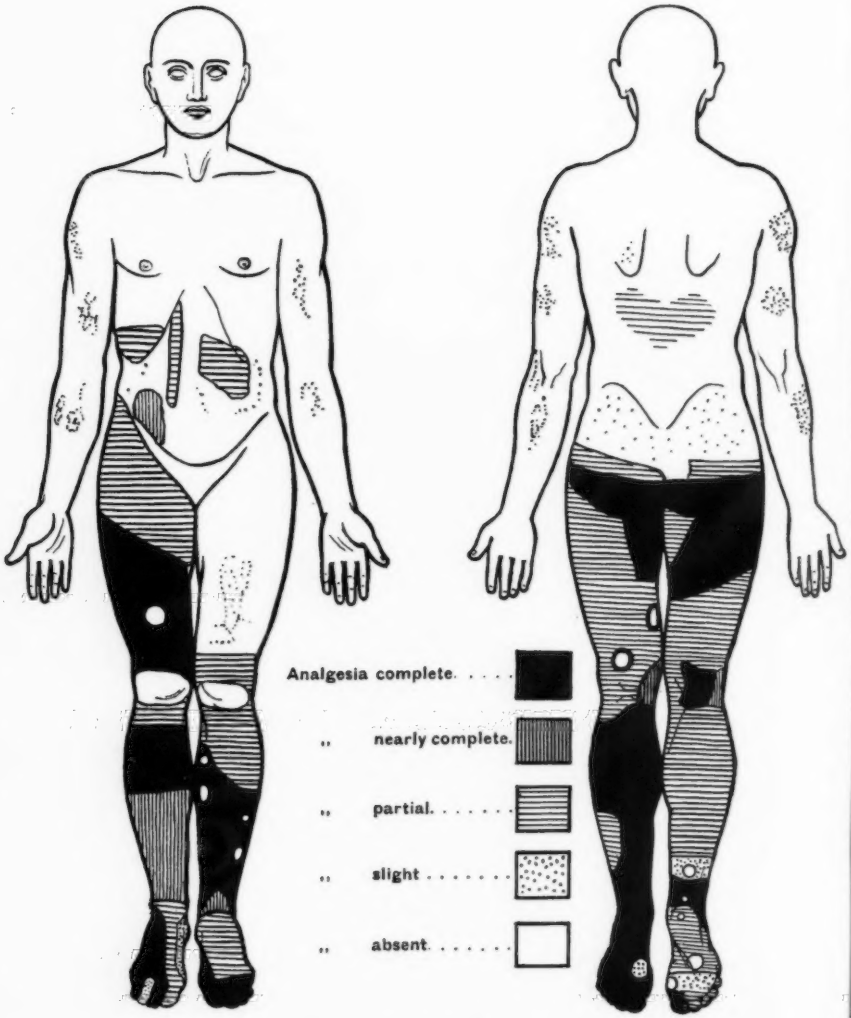


FIG. 1.—Diagram of areas of analgesia.

to the groin. It was traceable over part of the abdomen and, in a slight degree, over areas of the forearms and upper arms. On the posterior surface of both legs it extended in varying degree to the buttocks. In several places there were small patches of acute sensation surrounded by analgesic regions, as, for example, in front of both knees, in the front of the left leg, and on the soles of both feet.

(3) The knee-jerks were, as before, present but sluggish.

(4) The muscular power was certainly not below the average in any part of the body, though the patient complained that his muscles felt weak. There were no tremors.

(5) The smell and taste were normal.

(6) The sight of the right eye had become less clear. He complained much of a sensation as of dust moving in front of it. The light-reflex in this eye was sluggish. The pupil was smaller (*sic*) than that on the left side. The optic discs appeared normal, and no disease of choroid was observed; but there were marked opacities in the right vitreous humor, and the left was not quite clear.

(7) Shooting pains in the limbs had become more frequent. They occurred usually in the feet or toes, coming on suddenly without warning and being momentary but severe. He had occasional twitchings in the lumbar muscles.

(8) Drowsiness had become a marked feature of the disease during the last few months. He slept twelve hours out of the twenty-four, from eleven to eleven.

(9) The hearing was imperfect. At first he could hear a watch at 4 inches only on the right side, and 1 inch on the left. Some cerumen was removed: but this only caused an improvement up to 10 inches on the right, and $3\frac{1}{2}$ inches on the left side. The membranes appeared normal.

Up to this time all the symptoms observed, with the exception of the drowsiness (and perhaps the eye and ear symptoms), were referable to the spinal cord; there were none of the brain-troubles—the aphasia and paralysis—that had been observed in the three elder brothers. The patient had also lived to a greater age than any of his brothers; and the disease had been observed in him for two years without making very rapid progress. But in March, 1899,

he went out to a dance, and came home at three o'clock in the morning. He was unable to get a cab, and had to walk for two or three miles. Having been warned to avoid fatigue, he stayed in bed till one o'clock the next day; but while dressing he dropped a glass from his right hand, and found that he was unable to express himself clearly in words. He was seen by one of us within three-quarters of an hour of the commencement of the attack; the aphasia was then still marked, and he failed to read when asked to do so, no less than to converse. The attack had subsided an hour later, and he felt and seemed quite well in the evening.

He was again away, staying at Weymouth, during the greater part of the summer. On the whole, he had fair health while there; but in August (1899) he had two more attacks of temporary aphasia. Once also, after having been out in a boat (but without exposure to cold or wet) he was seized with severe pains in the folds of the buttocks, lasting about four hours. The pains came on about once a minute. He also had the afore-mentioned shooting-pains about once a month throughout the year, usually in the legs, sometimes in the hands. At the same time he gradually became weaker, and when seen in November (1899) had lost a good deal of flesh, especially in the lower limbs. The areas of analgesia were again mapped out, and were found to show very little variation from those of a year earlier. At this time, too, the eyes were examined by Mr. Lawford, who has kindly given us the following report on their condition.

October 16, 1899. Pupils dilated by homatropin and cocain.

V. R. $\frac{6}{36} \overset{+\ 0{\cdot}5\ \text{sphl.}}{-\ 2{\cdot}0\ \text{cyl.}} = \frac{6}{24}$.

L. $\frac{6}{18}$ vix $\overset{+\ 0{\cdot}5\ \text{sphl.}}{-\ 2{\cdot}5\ \text{cyl.}\ 15^{\circ}} = \frac{6}{18} \times \frac{6}{12}$ tried.

Fields of vision full. Ophthalmoscopically right and left no abnormal appearances detected in any part of fundus. Examination of right fundus much interfered with by vitreous opacity. Colour of O.D.'s healthy. Right cornea and lens clear. In vitreous there are numerous stringy, slowly moving opacities, chiefly about the middle of vitreous.

antero-posteriorly. They are all dark in appearance: no whitish bands seen. There is also much fine dust-like haze of vitreous. Left.—The changes in vitreous are very similar, but MUCH less obvious. The stringy opacities are about middle portion, but are few in number. Fundus can be easily and clearly seen.

When examined on a previous date without a mydriatic, the pupils were unequal and irregular. Right pupil oval, long axis horizontal: size 4 mm. Left pupil pyriform, size 6 mm. Actions of pupils to light very sluggish, and very small in amount; to accommodation fair, but less extensive than usual. Ocular movements and lid movements full. Tension normal.

The relatives were at this time anxious to try the effect of general massage, having seen the improvement produced in our patient's younger sister by Weir-Mitchell treatment; and a course was arranged for him, special care being taken to prevent his being over-tired. He was not seen again for a month. During that time he had become very distinctly worse. He had had about six attacks of aphasia, usually accompanied by temporary weakness in the right arm. In spite of this, however, he went out three consecutive evenings, and on the fourth day was so much worse that a doctor was again summoned. When seen he had not fully recovered from an attack of the preceding evening, his speech being imperfect, and the right grasp weaker than the left. His general weakness was now very great, and he could not be up for one hour without feeling fatigue. His memory and power of concentration were both feeble; the pulse usually rapid (90-100), the tongue absolutely dry. He complained of pain in his limbs of an aching character: the temperature was normal or subnormal. With rest, careful feeding, attention to the state of the bowels, and skilled nursing, he gradually recovered a certain amount of strength; and the attacks of aphasia, at first occurring every day, became less frequent. By February 20, 1900, he had been as much as ten days without an attack, and was able to be up for four or five hours without fatigue. During the spring and summer yet further improvement followed, and, while care-

fully avoiding all that tended towards over-exhaustion, he was able to move about freely out of doors, and to mix in society.

During the remainder of his life, the patient was under the care of Dr. R. Jocelyn Swan, to whom we are indebted for the following notes of that period. He lived for about nine months longer, and during that time had four convulsive attacks, in the last of which he died. "The first convulsive attack," Dr. Swan writes, "occurred on September 26, 1900, and lasted about twelve hours. A second similar seizure was on November 3, more violent and longer in duration, in all thirty-six hours. A third occurred on January 15, 1901, lasting nine hours, this was marked by a tonic contraction of the left arm, while the right moved aimlessly about, and the final attack was on May 24, commencing at 1 a.m., and lasting till he died at 9 a.m. of the same day." Dr. Swan adds that he continued to have "lightning-pains," especially at night; the two regions most affected being a spot on the outer side of the right foot below and in front of the external malleolus, and the folds of the buttocks. In the beginning of March he also had an attack of conjunctivitis of the right eye, which had become nearly blind; and there was some ulceration of the cornea leaving a nebula. It is not known whether the cornea had previously become anæsthetic; or whether the analgesia previously observed had extended over a larger area of the body.

II.

Pathological Note.

The *post-mortem* examination was made seventeen hours after death. The weather at the time was very warm. *Post-mortem* rigidity was well marked. There was considerable discoloration and lividity in the dependent parts. The head was opened first and on removal of the skull cap the dura was seen to be intensely congested. The venous sinuses were full and when the brain was removed blood oozed in considerable quantity from the spinal canal. In exposing

the spinal cord an abnormal density of bone in the vertebral laminæ was observed, notably in the lumbar region, and there was some extra-meningeal hæmorrhage in front of the cauda equina.

Thorax.

The heart was normal. The right lung was adherent at the apex from some old pleurisy, and in both it and in the left there was some patchy hypostatic consolidation and the lungs were markedly congested throughout. There was no sign of tuberculous disease.

Abdomen.

The liver and the spleen were both in a state of venous congestion.

The kidneys had their capsules readily separable and had also the appearance of congestion, though microscopically they seemed absolutely normal. The bladder was normal.

For microscopic examination, most of the organs were hardened in 10 per cent. formalin. Some of the cord, however, was placed in Müller's fluid.

For the nervous system, the staining methods were those of Nissl, van Giesen, Marchi and Weigert-Pal, along with others.

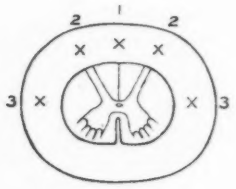
Spinal Cord and its Coverings.

Macroscopic.—The dura showed marked congestion. On reflection of the dura a rusty-coloured substance was seen to be present between it and the cord. This was gelatinous, stringy and friable, and in consistence suggested a fibrinous exudate. It formed a more or less complete sheathing to the cord throughout its entire length. It was, however, most abundant in the lower parts of the cord and was less so as the higher levels were reached, being in the neck almost absent. It was found chiefly on the posterior aspect and in some regions it separated the dura from the cord to the extent of a sixth of an inch or more. Anteriorly it was seen mainly as stringy masses about the anterior nerve roots. It was moderately adherent to the dura, but more

so to the cord itself, so that the former could without difficulty be raised, leaving the cord surrounded by its shaggy covering (fig. 2).

Microscopic.[1]—Examined under a low power. Sections taken from the level of the third cervical segment to the cauda equina all showed undue vascularity. This was not so striking in the cervical region, but got greater in lower levels, and became intense in lumbar and sacral regions. This vascularity affected chiefly the pial layer of the pia-arachnoid and the contents of the arachnoid space, viz., the nerve roots and the arachnoid tissue. But the vessels of the dura and the cord itself were also distended. The vessels seemed increased both in size and number. In the arachnoid space was a relatively large quantity of a fibrous material probably a hyperplasia of the normal fibrous trabeculæ. In general appearance it was similar to the fibres of the arachnoid tissue, but the cellular elements were fewer. It had the form of nodulated rods or fibres with a maximum diameter of about thirty times that of a red blood cell. There were also spheroidal bodies, though these probably were cross sections of the fibres. This tissue was found in different situations in the arachnoid space, among the nerve roots—sometimes actually among the nerve bundles of the roots—and more plentifully posteriorly.

There were usually aggregations of it in the following situations where normally a collection of arachnoid tissue might be expected:



[1] The terminology is that used by Ford Robertson by which *pia-arachnoid* is taken to mean the whole membrane, "pia," "arachnoid," and intervening tissue: and *arachnoid* is taken to mean the trabecular tissue which extends from the outer to the inner aspect of the membrane, thus, arachnoid trabeculæ, arachnoid spaces, arachnoid fluid.

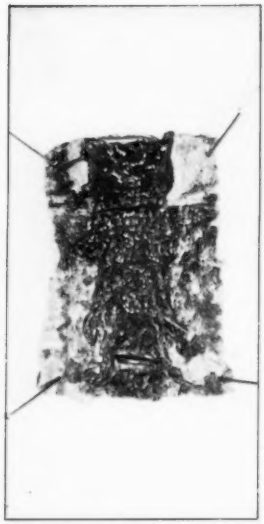


FIG. 2.—Portion of dorsal cord; posterior aspect, dura reflected.

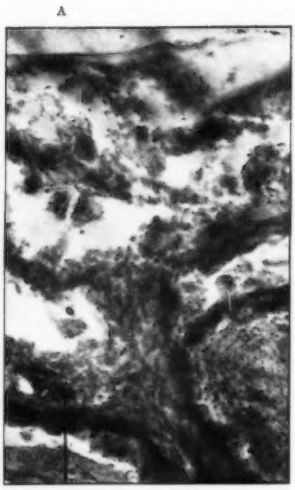


FIG. 3. — Photomicrograph. Mid-dorsal cord, transverse section, between posterior dura and cord (region about septum posticum). Hæmalum, × 105. *a*. Dura. *b*. Red blood cells. *c*. Arachnoid tissue.

FIG. 4.—Photomicrograph. Lumbar cord, transverse section, mass of arachnoid tissue, opposite one of the posterior roots. Hæmalum, × 60. *a*. Engorged blood-vessel. *b*. Hæmorrhage. *c*. Dura. *d*. Arachnoid tissue.

An aggregation at 1, presumably the septum posticum, was found chiefly in the higher regions: an aggregation at 2, chiefly in the lower regions. At 3, the position of the ligamentum denticulatum, there was an aggregation in all regions. The material was also present in the neighbourhood of the anterior fissure.

The fibres of this tissue had no definite arrangement, except in the above-mentioned groupings, but were disposed in all directions forming in places a loose network (figs. 3 and 4).

Under a high power they were seen to be fibrillar and with Weigert's fibrin stain they gave negative results. In the cauda equina it was present chiefly near the dura, but it was also to be seen among the nerve roots. In the interstices of this tissue collections of red blood cells were everywhere abundant, especially in the lower levels of the cord.

Stratified bodies (geschichtete Körperchen) were found in considerable numbers near the dura. The pial layer of the pia-arachnoid was much thickened. Its vessels were engorged, and in places there were hæmorrhages. There was in it an extensive round cell infiltration which invaded also the periphery of the cord itself, especially along the lines of the connective tissue septa and was marked in the neighbourhood of the posterior roots (fig. 5). The nerve roots presented the same appearance of intense congestion and round cell infiltration, and these conditions, though to a less extent, were also evident in the dura. In several of the smaller arteries there was distinct thickening of the intima presumably endarteritis. This was evident throughout the whole length of the anterior median artery. Thrombosis seemed to have taken place in several of the vessels in the more highly congested areas, and some of the thrombi were apparently undergoing organisation. The endarteritis did not affect the whole intima equally, being usually seen in transverse sections as an encroachment on one side of the lumen of the vessel (fig. 6).

Treated with the Weigert-Pal and Marchi staining methods the cord showed a degeneration in the posterior columns.

In the lower lumbar region the degenerated fibres were found mainly in the postero-external columns, but gradually as one passed up the cord they became more and more strictly limited to the postero-median columns. The degenerated fibres extended anteriorly in the postero-median columns as far as the gray commissure, except in the cervical region, where they only reached about one half of that distance. It was in fact exactly such a degeneration as would be occasioned by damage to the lower lumbar and sacral roots. In addition to this there was a marginal degeneration all round the cord, and extending to the parts bounding the anterior fissure (fig. 7).

Sections through the upper part of the cauda equina treated with the Weigert-Pal method showed many of the roots much degenerated.

The nerve cells in sections taken at many levels of the cord treated by Nissl's method, appeared absolutely normal. There was no evidence of chromatolysis or other degenerative change. The chromophile substance, as represented by the "Nissl-bodies" seemed normal in quantity, arrangement and staining reaction. This applies to cells in all situations—in anterior and lateral horns and Clarke's column. In a few cells there was a deeply staining nucleus, but this was taken to be a *post-mortem* change. Beyond engorgement, the vessels of the cord itself were not affected. There was no perivascular round cell infiltration. Concentric bodies, giving "amyloid reaction," were present in the white matter in moderate numbers.

Brain and its Coverings.

Macroscopic: The dura showed great congestion. It being reflected, the surface of the brain was seen to be intensely congested, especially over its convexity, while covering the medulla and base of brain, was found what appeared to be the same gelatinous, friable substance already described as surrounding the cord. The pia-arachnoid was cloudy and thickened over Sylvian fissures, and on opening up the latter, the same substance was found filling them up and causing the two sides to be adherent.

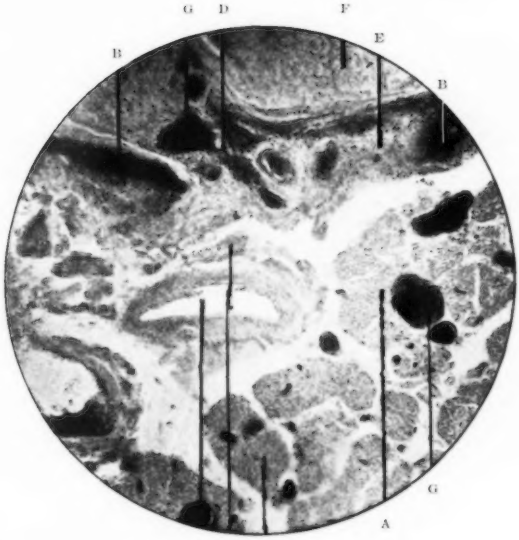


FIG. 5.—Photomicrograph. Sacral cord, region about anterior fissure. Hæmalum, × 60. *a*. Nerve roots. *b*. Dilated blood-vessels, possibly hæmorrhage. *c*. Artery with thickened intima. *d*. Inflammatory infiltration in anterior fissure. *e*. Thickened pial layer of pia-arachnoid. *f*. White matter of cord. *g*. Dilated blood-vessels. *h*. Arachnoid tissue.

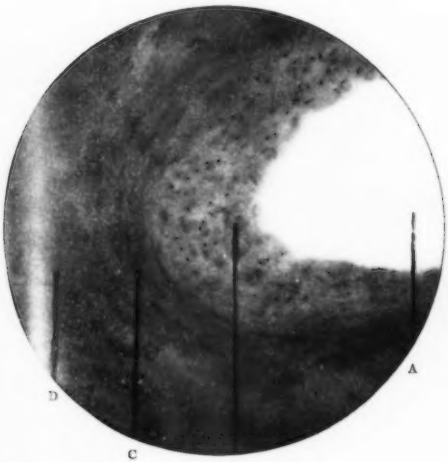


FIG. 6.—Photomicrograph. Lumbar cord, transverse section of anterior median artery. Hæmalum, × 270. *a*. Lumen of vessel. *b*. Thickened intima. *c*. Media. *d*. Adventitia. N.B.—This appearance is not due to obliquity of section.

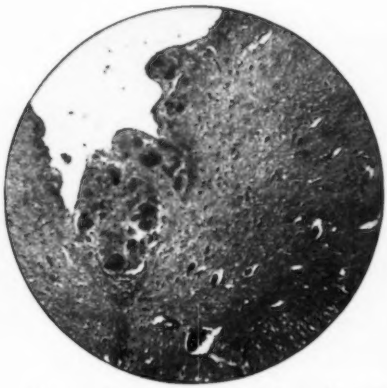


FIG. 8.—Photomicrograph. Floor of fourth ventricle in pons, showing "hyaline" bodies, Van Giesen, high power.

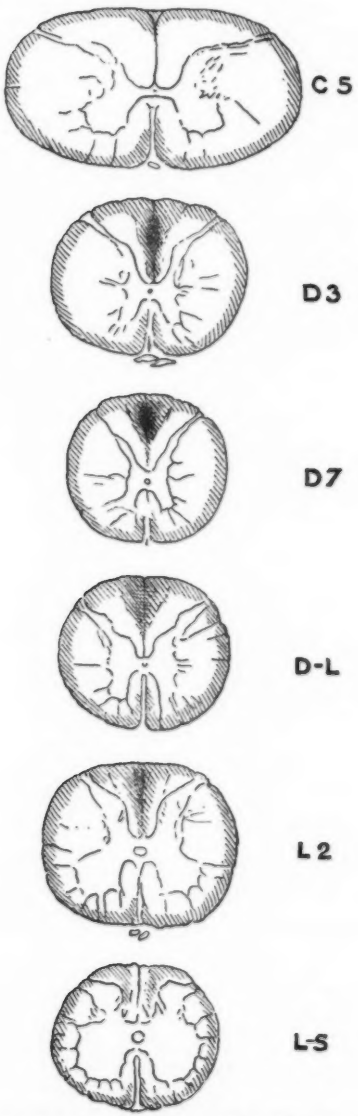


FIG. 7.—Drawing from sections prepared by the Weigert-Pal method to show cord degeneration.

It was also present between the two frontal lobes below the corpus callosum, making them adherent, and surrounding the anterior cerebral arteries and their branches. The pia-arachnoid did not separate easily from the cortex. In all other respects, the brain appeared quite normal. The left Sylvian artery with its main branches contained clot, but this was red and non-adherent, and probably *post mortem*. Recent clot was present also in several other branches of the circle of Willis.

Microscopic.—Sections were made through Basilar artery, both Sylvians, both anterior cerebrals and posterior communicatings. All were found perfectly normal with the exception of the first, which showed very slight endarteritis.

Sections of the third left frontal convolution, and of many other parts of the cortex were examined. There were practically the same appearances in all. There was a fibrous hyperplasia of the arachnoid tissue, with increased vascularity. The cortical arterioles were normal. The cortical nerve-cells were likewise normal, examined by Nissl's method. Many however, had the deeply staining nucleus and indistinct chromophile substance, described by Ford Robertson as *post-mortem* change.

Sections of the left internal capsule and of the corpora striata were also examined with portions of the white matter from various other regions, and all seemed quite normal.

Sections through the medulla and pons showed the nerve-cells at the floor of the fourth ventricle normal, and the same appearance of the pia-arachnoid, as was seen on the cord.

In the medulla and pons, immediately subjacent to the ependyma lining the fourth ventricle, were numerous, roundish, homogeneous, hyaline-looking bodies with concentric markings, not staining very deeply with methylene blue, and about ten or fifteen times the diameter of a red blood cell. These bodies did not blacken with osmic acid, nor did they give the "amyloid reaction" with iodine, or iodine and sulphuric acid (figs. 8, 9, 10).

These bodies were not present under the ependyma of the lateral ventricle. The cerebellum was normal.

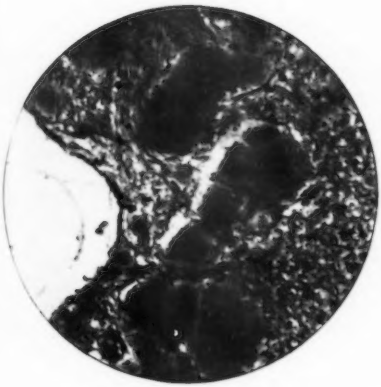


FIG. 9.—The same, low power.

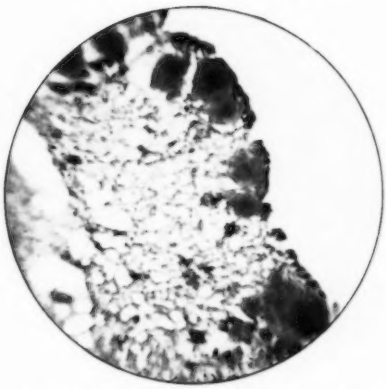


FIG. 10.—Photomicrograph. Floor of the fourth ventricle in medulla, at level of hypoglossal nucleus, showing "hyaline" bodies, Van Giesen, × 370.

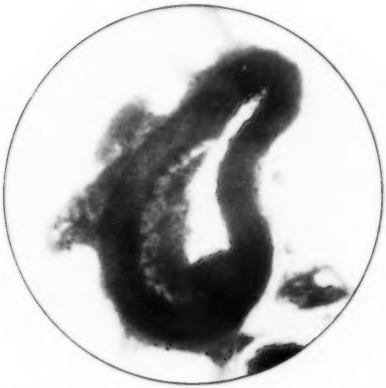


FIG. 11.—Photomicrograph. Artery from great sciatic nerve, showing thickened intima. Hæmalum, × 270.

Peripheral Nerves.

The peripheral nerves as represented by the ulnar and great sciatic were examined by the Marchi and Weigert-Pal methods, and were found to be normal, showing no sign of either neuritis or degeneration. Some of the arteries, however, in the great sciatic had the same thickened intima already described in the vessels of the cord (fig. 11).

The Eye.

The right eye was embedded in celloidin, and it was examined in antero-posterior sections. There was no direct evidence of choroiditis, but in the posterior chamber there was a considerable quantity of filmy, fibrinous looking material. The eye in other respects appeared normal.

The condition thus seems to have been primarily a spinal lepto-meningitis extending from below upward until the cerebral meninges were affected in a like manner, chronic in its course, but intense enough to implicate the cord superficially, and many of the nerve-roots in the inflammatory process.

The great vascularity and numerous hæmorrhages in the inflamed area suggest an inflammation hæmorrhagic in type, and the excess of arachnoid tissue suggests that this constituent of the pia-arachnoid was especially involved.

The tract degeneration in the cord is manifestly the result of damage to the lower posterior roots. The bodies in the floor of the fourth ventricle are not fatty, and not amyloid as is seen by their staining reaction. They seem to belong to the group of hyaline bodies.

Our best thanks are due to Dr. Lazarus-Barlow for many kind suggestions, and for allowing us to make use of the pathological laboratory of Westminster Hospital during the preparation of this part of our paper.

We have found among other works the following of particular service :—

KEY AND RETZIUS. "Studien in der Anatomie des Nervensystems, &c."
OBERSTEINER AND HILL. "Anatomy of Central Nervous System."
FORD ROBERTSON. "Pathology of Mental Diseases, 1900"; and "Normal and Pathological Histology of Nerve-Cell," BRAIN, 1899.

POLLACK (JACK). "Methods of Staining the Central Nervous System," 1899.
MOTT. "Tabes dorsalis"; Clifford Allbutt, "System of Medicine," vol. vii.

III.

Before considering the nature of the disease we may here review shortly some of the more prominent symptoms, and consider in what degree they may be accounted for by the lesions above described.

(1) *The Bladder Symptoms* occurred in three out of the four males who suffered from the disease. With regard to the three females of the earlier generation no mention is made of this symptom, but the records concerning them are not full enough to justify us in concluding from this that the bladder was unaffected. Usually the nocturnal escape of urine was the first symptom in the disease to attract the attention of the patient himself, and in the earlier stages of the male cases it was regarded as an isolated symptom, like the incontinence of children, and treated with belladonna, &c. Later, however, the bladder becomes undoubtedly atonic, urine is retained in the bladder, and cystitis is set up, and in the light of the fuller knowledge of the last case that we now possess there can be little doubt that the primary defect is *retention* due to some fault in the nervous mechanism of micturition.[1] When we first saw our patient the bladder walls had already become very considerably weakened. He could expel very little urine with any force, the remainder trickling slowly away; the catheter showed several ounces of residual urine, after the first free flow of urine had ceased; pus and albumen were present, and disappeared when the bladder was regularly washed out. At this time he was having what he called "incontinence of urine" every night, and the most probable cause for this is that the bladder was only half empty when he went to bed, in a few hours it became full to its utmost capacity, and then discharged a certain portion of its contents, either by

[1] J. RISIEN RUSSELL (Clifford Allbutt "System of Medicine," vi., 877), says that in affections of the spinal meninges retention is common, incontinence also occurs, though more rarely.

reflex stimulation of the lumbar centre or by simple overflow. Later in the disease all power of voluntary micturition was lost, and the bladder was emptied at regular intervals by the catheter, this prevented over-distension from occurring, and the so-called incontinence now disappeared. Three nervous lesions suggest themselves as possible causes for this retention :

(1) Disturbance of the lumbar centre for micturition.

(2) Disease of the white fibres in the lumbar or dorsal region, carrying impulses from the brain to the centre.

(3) Analgesia of the bladder, similar to that existing in the legs, allowing distension to occur frequently without discomfort, and in time to weaken the muscular fibres of the bladder wall.

(1) *Disturbance of the Lumbar Centre.*

The cord has suffered considerable damage in the region of the lumbar enlargement, enough possibly to account for imperfect action of the centre, and this explanation of the symptom is tempting, inasmuch as similar damage to neighbouring centres would account both for the constipation and for the loss of sexual power. But the early symptoms suggest that the centre is cut off from the usual stimuli rather than that it fails to act in response to them, and the later stages of disease of the centre should cause paralysis of the sphincter, with continuous overflow, rather than retention.

(2) *Disease of the Descending Tracts above the Lumbar Centre.*

A lesion of this nature would cause retention of urine, and a series of symptoms not unlike those observed ; but no such lesion has been discovered on examination of the cord ; and the absence of discomfort when the bladder was distended is hard to explain. It is possible, however, that this might be attributable to further damage elsewhere, *e.g.*, in the posterior roots.

(3) *Analgesia of the Bladder Wall.*

A failure to perceive the pain and discomfort normally felt when the bladder is over-distended might lead to a condition such as has been described; and it is known that retention sometimes occurs in syringomyelia.[1] If, however, the cause lies here, it will, no doubt, have been at work long before the first escape of urine; indeed, dissociated anæsthesia will be the first symptom of the disease. The sequence of events would be as follows:—The patient allows his bladder to be over-distended on many occasions without feeling the discomfort that would trouble a healthy man;[2] the bladder becomes distended, weakened, atonic; then it is incompletely emptied, and cystitis occurs. Finally, it loses all muscular power, and no longer responds even to the reflex stimulus of great distension.[3]

It does not seem impossible that more than one of these agencies may have been effective in producing the symptoms described.

Opacity of the Vitreous Tumour of the Eye.

This was present in two out of the three patients in the earlier generation, and in two out of the five in the later generation; while in the others we have no record as to the presence or absence of the trouble. The constant lesion consists in vitreous opacities, the appearance of which has been carefully described for us by Mr. Lawford; almost complete blindness may follow, as occurred in the mother of patient. A variation in the size and shape of the pupils has also been observed in the latest of the cases. No hæmorrhages within the eyeball have at any time been seen, and no choroiditis was observed in that part of the choroid that

[1] Ref. WALTER VOUGHT, "Syringo-myelia and Allied Diseases." *N.Y.M.J.*, November 21, 1891.

[2] It is possible that the penile pain felt a week before the first voluntary escape of urine was caused by great pressure on the neck of the bladder, which still retained some pain sense.

[3] J. RISIEN RUSSELL (Clifford Allbutt "System of Medicine," vol. vi., p. 877) has described residual anæsthesia as being especially common in the bladder and rectum in affections of the Spinal Meninges.

can be examined with the ophthalmoscope; but it is most probable that the primary cause of the opacities is hæmorrhagic, and it is possible that disease may have been present in the anterior portion of the choroid, or other parts of the uveal tract, though, as has been pointed out, no evidence of this was found microscopically.

The disturbance of the sense of heat and pain, along with unimpaired tactile sensation, seems to point to the probability suggested by Gowers[1] that the paths of conduction of heat and pain sensation are close together, but are widely separated from the path conducting tactile impressions.

It has been suggested by Starr[2] that on their way from the surface of the body the sensations of heat and pain traverse the gray matter and then go on in the centripetal fibres of the antero-lateral-ascending tract of Gowers. If this is so it might well be that the disturbance of heat and pain sense was due to the implication of this tract in the marginal myelitis which we have seen to be present, the gray matter being to all appearance normal.

With regard to the cerebral symptoms, drowsiness, impaired hearing, aphasia, right-sided hemiplegia, loss of memory and power of concentration, convulsive attacks and coma, we would suggest that they were due to a condition of cerebral anæmia caused, in the first place by venous congestion associated with the inflamed meninges interfering with the normal arterial blood supply; and in the second place by actual compression of the arteries by the new inflammatory material.

The latter might account for any local increase of the anæmia, such as that capable of causing aphasia or hemiplegia, and indeed the quantity of new material found in the Sylvian fissures and elsewhere at the base of the brain, matting everything together, makes this hypothesis not very improbable.

This does not, however, explain the transitory nature of the attacks of aphasia and paralysis.

[1] "Diseases of the Nervous System," vol. i., pp. 235, 237.
[2] Clifford Allbutt, "System of Medicine," vol. vii.

Finally, a few suggestions may be made with regard to the nature of the disease, which we have described. We think that it will be admitted that the consistent grouping of symptoms is sufficiently marked to constitute the disease a definite entity; and that in character it corresponds to no form of hereditary nervous disease that has hitherto been described.

There is, however, a superficial resemblance to some of the known diseases. Thus, it resembles syringomyelia in the one symptom of dissociated anæsthesia; and it is also like this disease (as well as certain other hereditary affections, *e.g.*, hereditary chorea, hereditary cerebellar ataxy, and hereditary ataxic paraplegia) in the late onset of the symptoms, after a healthy childhood and youth. There is a closer resemblance to locomotor ataxia in the lightning-pains, the diminution of knee-jerks and of light-reflex, and in one actual lesion found *i.e.*, the posterior sclerosis (though this symptom in our case was presumably secondary to the pia-arachnitis): while both locomotor ataxia[1] and Friedreich's ataxia[2] may be accompanied by dissociated anæsthesia and impairment of the sexual and bladder functions.

Now there is strong reason to believe that there is a close connection between locomotor ataxia and syphilis and the pathological evidence that has arisen in the investigation of the last case suggests the possibility of the disease being caused by the action of the virus of hereditary syphilis on the structures surrounding the spinal cord. The likelihood of this factor was considered during the lifetime of the patient; but was put aside because no satisfactory evidence existed that syphilis could involve three successive generations;[3] but that this objection is not final must be admitted in consideration of the following facts:—

[1] Clifford Allbutt, "System of Medicine," vii., 116.
[2] "Gowers," 1892, 1st Edit., 464.
[3] J. Hutchinson (Clifford Allbutt, "System of Medicine," ii., 263) says that no facts have yet been published on this subject. Out of eight families investigated in which the parents had suffered from hereditary syphilis, there were no syphilitic offspring "with one doubtful exception." He adds, however, that "several surgeons have expressed the belief that the influence of syphilis once acquired may be felt through several subsequent generations."

(1) The vascular pia-arachnitis, closely resembling that found in syphilitic meningo-myelitis.[1]

(2) The thickening of the tunica intima in some arteries similar to that found in syphilis.

(3) The ocular lesions, which suggest former hæmorrhages like those of syphilitic choroiditis.

(4) The thickening of the neural arches in the lumbar region, found at the *post-mortem* examination.

(5) The character and duration of the disease from which the grandfather died ("gangrene" of lung lasting four months), and his dissipated life.

(6) The frequent occurrence of temporary attacks of aphasia in cerebral syphilis.

(7) The diminution of pain-sense and temperature-sense,[2] common in syphilitic meningo-myelitis.

We therefore suggest that this may be yet another manifestation of this polymorphic disease; though it is impossible to say why the virus should have selected these special regions, while producing none of the better-known symptoms that accompany the hereditary form of the disease.

[1] *Vide* OPPENHEIM (Mayer) "Text-book of Nervous Diseases"; RISIEN RUSSELL, Clifford Allbutt, "System of Medicine," vi.; ZIEGLER, "Special Path. Anat.," &c.

[2] Clifford Allbutt, "System of Medicine," vi., 895.

CASE OF EXTERNAL SPINAL PACHYMENINGITIS, IMPLICATING THE ENTIRE VENTRAL SURFACE OF THE SPINAL DURA.

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EXTERNAL spinal pachymeningitis, except the tuberculous variety of limited extent, is uncommon, and, so far as we know, no case of external spinal pachymeningitis is on record in which the entire ventral surface of the dura, from the foramen magnum to the caudal end of the dural sheath, was adherent to the bodies of the vertebræ by fibrous proliferations, and the rest of the spinal dura was normal. Such a case forms the subject of this paper.

A man, white, 42 years old, piano-tuner by occupation, was admitted to the Philadelphia Hospital, February 17, 1896. No family history of importance was obtained except that two brothers and three sisters died in childhood. The patient had been blind since he was three months old. During his early life he had scarlet fever, pneumonia, typhoid fever, and rheumatism. He drank moderately, and denied venereal disease.

In June, 1895, he, for the first time, had a feeling of numbness in the right great toe. This numbness, after gradually spreading to the knee, attacked the other foot and

leg in the same way. He had no pain, but the numb limbs felt as if asleep. Previous to the numbness he had had, for a time not fixed, some swelling and tenderness in the legs, and an aching pain in the lumbar region. He could walk until November, 1895, but his knees became bent (probably from spasticity), and he felt as if walking on springs. He began to have nocturnal incontinence of urine in July, 1895.

On February 21, 1896, a few days after admission, the record was made of exaggerated reflexes in the lower extremities, with a tendency towards a spastic condition. Ankle clonus was marked in both feet. It is to be inferred that the condition noted as having developed between July and November, 1895, was still present, namely, numbness in the lower extremities, inability to stand and walk, and incontinence of urine. His heart and vessels were described as normal, lung expansion was good, and respiratory murmur was normal. His bowels were constipated. On October 12, 1898, a note was made that sensation was intact, that the knee-jerks were plus when the muscles were relaxed, and that ankle clonus was not present, possibly on account of rigidity. Ward notes made on November 29, 1900, stated that the legs became rigid on effort; the patient could extend his lower limbs and stand, but could not walk; the knee-jerks were excessively exaggerated, and the irritation, in taking this reflex, provoked spasms of the legs in extension. Both legs also became firmly adducted; the feet were spastic at the ankles; no ankle clonus could be elicited; the Babinski reflex was typical and decided on both sides; sensation was everywhere well preserved; the legs appeared to be hypersensitive.

On April 17, 1901, it was noted that his right hand had been cyanotic and painful for some time. Signs of gangrene began to appear on two fingers of the hand. The patient was transferred from the nervous wards to the surgical wards for treatment. As the gangrene was evidently spreading, and as the patient suffered excruciating pain, amputation of the right hand was performed April 18, 1901. So far as the operation was concerned the patient in all respects did well. On May 9, 1901, he complained of severe pain in the left

side, and auscultation revealed some suggestion of a friction sound. The temperature rose, and pulse and respiration increased. On the 10th dulness over the left lobe was observed, and breathing sounds were harsh. His active lung symptoms gradually subsided, and he was retransferred to the nervous wards. On June 22, 1901, he again complained of pain in the left side. On examination a fairly superficial friction rub was heard in the mid-axillary line on the left side, from about the fifth to the seventh rib. At the angle of the left scapula was an area in which expiration was shortened and harsh. The whole left base was dull and breathing sounds and expansion were much decreased; fremitus was not markedly altered. The patient's pulmonary condition again improved, and he remained in fair health until December. He was troubled from time to time with dyspnœa, and in October had an attack of copious hæmoptysis. On December 7, 1901, he was attacked with severe dyspnœa. Breathing was laboured and frequent, and speaking was difficult. Expansion was limited on both sides. He grew rapidly worse, and died on December 8, with œdema of both lungs. The symptoms referable to the nervous system remained practically the same during the last year or two of the man's life. He was frequently seen by one of us (Dr. Mills) during his term of service. The patient's condition from the notes already given and from recollection can be summarized as follows: He was paralysed in both lower extremities, and these were the seat of spasticity and marked contractures; all the deep and superficial reflexes in the lower extremities were much exaggerated, and he suffered from incontinence of urine; objective sensation was everywhere intact as late as November 29, 1900.

The necropsy was made December 8, 1901. It revealed many interesting pathological conditions in various parts of the body which, with the exception of the condition of the spinal dura and spinal cord, need only be briefly summarized here as follows: Thrombosis of the right pulmonary artery, cardiac dilatation, miliary tuberculosis and œdema of the lungs, parenchymatous nephritis and arteriosclerosis.

The external surface of the spinal dura on the ventral

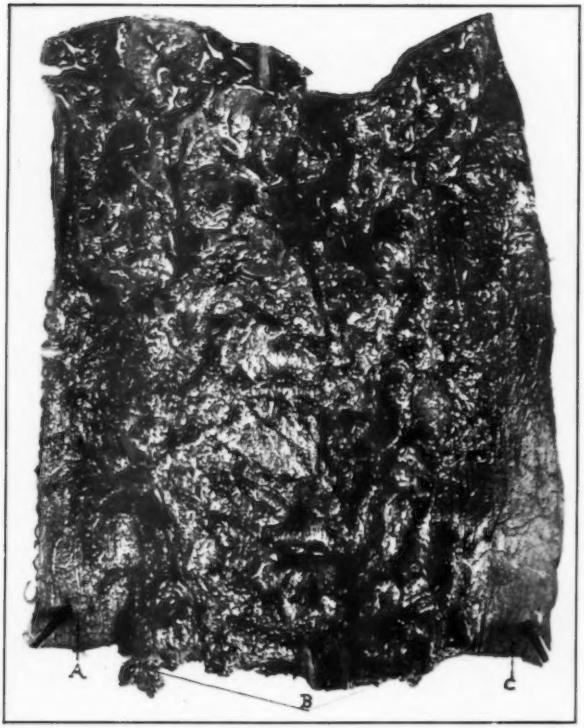

FIG. 1.

Photograph of the external surface of a part of the spinal dura.

The dura has been cut through in the dorsal portion. *A.C.* Dorsal portion of dura. *B.* Ventral portion of dura showing proliferation.

aspect was firmly adherent to the bodies of the vertebræ throughout the spinal canal. The dorsal aspect of the dura presented nothing abnormal, a single transection of the cord made between the tenth and the eleventh thoracic roots showed a gelatinous appearance to the naked eye in the crossed pyramidal tracts.

Microscopical examination reveals the following conditions :—

Sections from the right and left paracentral lobules appear to be normal, as do also sections from the medulla, except that the blood-vessels are distended.

Most of the nerve-cell bodies of the lower cervical region are well developed, although some appear atrophied, and here and there a few nerve-cell bodies in which the nucleus is displaced are found. Some small hæmorrhages of recent date are seen within the sections. The columns of Goll in the cervical region are much degenerated, and the degeneration is such as results from a lesion lower in the spinal cord. The ventral and dorsal roots appear to be normal. The direct cerebellar tract and the tract of Gowers on each side are degenerated. The crossed pyramidal tracts contain a slight excess of neuroglia, but by Weigert's hæmatoxylin stain do not appear degenerated. No signs of leptomeningitis are detected.

In the mid-thoracic region the degeneration is very intense, especially in the peripheral portions of the cord. Only the nerve-fibres near the central gray matter are intact. The anterior and posterior roots do not stain well, partly on account of the method of hardening, and it is difficult to decide concerning the condition of these roots. There is no evidence of leptomeningitis.

In the lumbar region the nerve-cell bodies seem to be normal. The crossed pyramidal tracts are degenerated, and the degeneration extends forward at the periphery of the cord, beyond the usual area of these tracts. The posterior columns are also partially degenerated. The condition of the anterior and posterior roots cannot be positively determined, as the roots do not stain well.

The dura, in its ventral portion, is composed of the

fibrous tissue commonly found in this sheath, and the proliferations on the outer part of the dura are composed chiefly of the same fibrous tissue. At one place a small collection of cells with round nuclei, separated into groups by bands of fibrous tissue, is found, but collections of these cells with round nuclei are rare in the proliferations from the dura, and there is little evidence of acute inflammation. At some places what appears to be metastatic bone formation is found in the proliferations on the dura.

One of the ulnar nerves contains much excess of connective tissue between the nerve-bundles, and some of the nerve-bundles are partially degenerated. One of the musculospiral, one of the median, and one of the plantar nerves are in a similar condition.

A piece of muscle from the sole of the foot appears considerably atrophied, and numerous round nuclei are found in places between the muscular fibres, so that in these places myositis existed.

The eyeballs were examined by Dr. E. A. Shumway, whose report is as follows: "The smaller eye shows phthisis bulbi, with extensive bone formation in the interior of the eye, in the exudate on the choroid; nerve atrophic. The larger eye shows thick leucoma of cornea, staphyloma beginning; cornea entirely cicatricial; iris and ciliary bodies atrophied to a high degree; iris adherent to cornea throughout; organised tissue anteriorily due to old choroiditis; retina and choroid show chronic inflammation, with secondary pigmentation of the retina; optic nerve head deeply excavated, entirely atrophic."

Chronic external pachymeningitis of the cerebral dura is so rare that Alexis Thomson,[1] in 1894, said he had not been able to find the record of any specimen but that of the two which had come under his own observation. Lannelongue he mentions as having met with the condition while performing craniectomy in a case. One of Thomson's cases was in a child aged five years, who had died of abdominal tuberculosis. There was no sign or history of rickets or syphilis. The dura was firmly adherent to the calvarium,

[1] Alexis Thomson, *The Journal of Pathology and Bacteriology*, vol. ii., 1894.

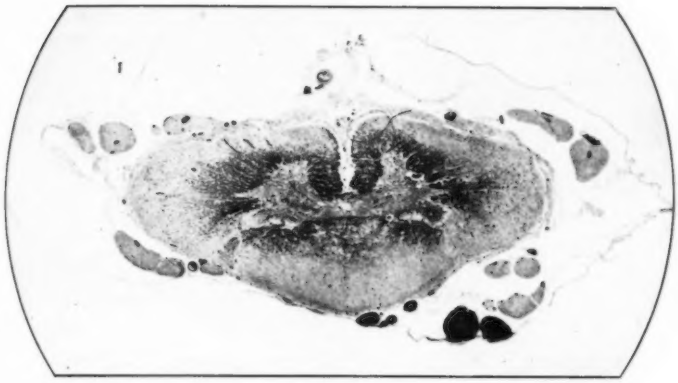

FIG. 2.

Photograph of a section from the mid-thoracic region.

The degeneration is intense in the peripheral portions of the cord.

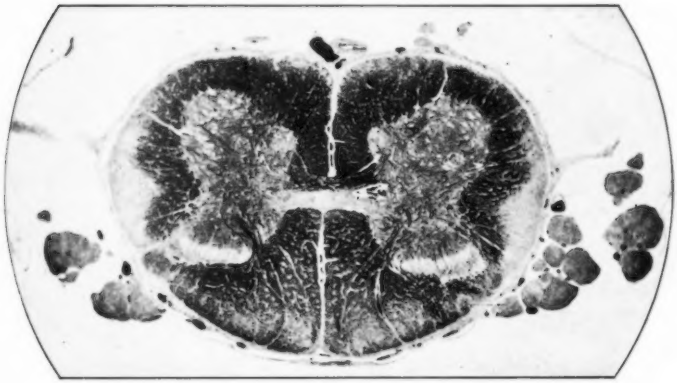

FIG. 3.

Photograph of a section from the lumbar region.

The crossed pyramidal tracts are degenerated, and the degeneration extends forward beyond the area of these tracts. The posterior columns are also partially degenerated.

and on being forcibly torn from the bone presented on its outer surface a uniform layer of red sprouting granulations or villous processes. The inner table of the skull presented an infinite number of grooves and pits in which the granulations were embedded. The lesion was confined to the outer aspect of the dura in the region of the parietal eminences, and was perfectly symmetrical on the two sides, the cerebral surface of the dura being normal. Each process on the outer surface of the dura was made up of one or more capillary loops, surrounded by numbers of cells, the majority of which were leucocytes. Among these were a few scattered spindle-shaped corpuscles, and here and there clumps of red blood corpuscles. The cells and vessels were feebly supported by a very delicate recticulum of fibrin.

The second specimen was found by Thomson in a museum.

Thomson believed that the characteristic features of the pathological process in these cases depended upon a reversal of the normal function of the dura, regarded in its capacity as an internal periosteum of the skull. Bone formation was replaced by the projection of vascular loops from the dura against the bone, leading to progressive softening of the latter, and the process was exactly like the method of absorption met with in inflammation (periostitis and osteomyelitis). Thomson says it was noteworthy that while the external surface of the dura was thickly studded with vascular granulations, there was scarcely any evidence of increased vascularity or of inflammatory changes in the substance of the dura. He regards the process as an aberration of development rather than as an inflammation. It caused no symptoms and showed no evidence of its existence during life.

External spinal pachymeningitis of non-tuberculous nature of limited extent has been occasionally observed. Stoubell's,[1] for example, reports a case of syphilitic external spinal pachymeningitis. A woman, aged 86, during one night became paraplegic in both lower limbs, and was anæsthetic as high as the umbilicus. The patellar

[1] STOUBELL, *Neurologisches Centralblatt*, 1898, p. 1, 120.

reflexes were absent, and there was no ankle clonus. Death occurred two and a half weeks later from pneumonia. At the necropsy the thoracic vertebræ from the third to the sixth were found diseased, and the meninges in this region were thickened. A microscopical examination showed that the process was neither tuberculous nor carcinomatous. The meningeal growth had its origin from the outer surface of the dura, and was anteriorly united with the periosteum of the vertebral canal. It consisted of small-cell granulation tissue. The process was believed to be syphilitic. Stoubell remarks that syphilitic external pachymeningitis (peri-pachymeningitis) is extremely rare, and refers to cases reported by Virchow and Heubner.

In the case described in this contribution, no disease of the vertebræ, to explain the adherence of the spinal dura to the bodies of the vertebræ, could be found at the necropsy, although no vertebral bodies were removed, and yet this adherence was so great that a knife was constantly employed to cut through the proliferation during the removal of the spinal cord and dura, and these proliferations consisted of dense fibrous tissue.

The degeneration of the posterior columns was probably caused in part by the degeneration of the posterior roots which were doubtless compressed by the abnormal fibrous tissue on the outer surface of the dura. Internal pachymeningitis or leptomeningitis did not exist anywhere. The intense degeneration of the thoracic region, especially of the mid-thoracic region, is difficult to explain. The spinal cord in the mid-thoracic region was very small, and the peripheral portions were entirely degenerated. The vertebral canal in the thoracic region is smaller than in the cervical or lumbar region, and if there were any œdema of the spinal cord, or any increase in the amount of the cerebro-spinal fluid, the effect of this pressure on a spinal cord firmly adherent by its dura to the bodies of the vertebræ might be most distinct in the thoracic region. The changes of the spinal cord in this region were such as might be produced by interference with the circulation and by pressure, and yet the nature of this pressure is not very evident, as the

adhesions alone were hardly sufficient. The degeneration of the white columns of the cervical region was secondary to that of the thoracic region, as was also in part that of the lumbar region.

The degeneration of the peripheral nerves was probably caused by the involvement of the nerve-fibres, in passing through the thickened dura.

We cannot determine the nature of this external spinal pachymeningitis. There was very little evidence of acute inflammation, and the tissue forming the proliferations was chiefly of a fibrous character, and resembled closely that of the dura. It is possible that the process was syphilitic; but, if so, it was of a character very unlike that usually found in syphilitic lesions. Syphilis, when it occurs within the vertebral canal, usually causes a meningomyelitis, but there was not the slightest evidence of such a process in this case. The characteristic lesions of tuberculosis were not found within the vertebral canal. The external spinal pachymeningitis probably existed some time before it caused symptoms.

Such adhesions as existed in this case might have caused rigidity of the spinal column, but that does not appear to have been present. It seems remarkable that objective sensation was everywhere intact as late as November 29, 1900. It is possible that at that date very careful examination might have revealed some slight diminution in sensation, especially of the thorax or abdomen; it is also possible that the degeneration of the thoracic region of the spinal cord increased greatly during the last year of the patient's life, during which time no observation concerning sensation was recorded.

ON CHANGES IN THE CENTRAL NERVOUS SYSTEM IN THE NEURITIC DISORDERS OF CHRONIC ALCOHOLISM.[1]

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It is now well known that in alcoholic paralysis, as in other forms of toxic neuritis, the degeneration of peripheral nerve-fibres does not stand alone, but is associated with a more or less characteristic type of change in the related nerve-cells. Moreover, in recent years observations have been reported which tend to show that this combination of fibre degeneration with cell change is, at least in many acute cases of the disease, not confined to neurones which go to make up peripheral nerves, but is exhibited also by neurones of various groups situated entirely within the brain and cord. The disease is something more than a mere peripheral neuritis, and represents a very wide-spread affection of the whole nervous system. Not only does it appear to be allied to certain spinal degenerations, but it stands in intimate clinical and pathological relationship with a number of important cerebral disorders in which there may be no appreciable peripheral affection.

During three years in which I was a medical officer at Colney Hatch Asylum, there came under my observation fifteen cases of alcoholic neuritis, and in three of these I had an opportunity of making a pathological examination. The observations are here recorded. A more detailed account of case 1 will shortly appear, with illustrations, in vol. ii. of the "Archives of Neurology" of the London County

[1] Abridged and adapted from a thesis for the Oxford M.D. degree.

Asylums. A comparative study of that case with the two others subsequently investigated, is however of sufficient interest to induce me here to give a brief abstract of it. For the three cases present not only important resemblances, but also instructive differences, so that much of their significance becomes apparent only when they are examined side by side.

The observations here recorded suggest: (1) That the peripheral and central lesions express a nervous degeneration of toxic origin, in the production of which no essential part is played by changes in interstitial tissues supporting the nervous structures, or by changes in the blood vessels concerned with their nutrition. (2) The changes in the nerve-cells are not the mere result of antecedent damage of nerve-fibres, but the changes in the fibres and cells together express a highly selective affection of whole neurones. (3) The peripheral neuritis is simply a local expression of this affection, and is not of purely local and peripheral causation. (4) The lesion of peripheral neurones is only one of many manifestations of the disease, and is accompanied by lesions identical in nature, affecting many groups of neurones situated entirely within the central nervous system. (5) The central changes are not attributable to the peripheral neuritis, and though in some cases the peripheral neurones are mainly affected, in others the morbid process chiefly implicates central neurones; but these two groups of cases do not appear to be sharply divided.

CASE 1.—*Acute alcoholic paralysis, fatal after six weeks duration, and presenting all the usual clinical and pathological evidences of acute degeneration of cranial and spinal nerves. "Polyneuritic" mental disorder. Death from vagus paralysis and heart failure. No appreciable vascular changes in nervous system. Acute cell changes in cord, spinal ganglia, medulla and cortex. Degeneration of pyramidal tracts, fronto-thalamic fibres, and the exogenous fibres of the posterior columns.*

Well-developed, well-nourished woman, aged 32, married. History of eight years' excessive gin-drinking; several attacks of delirium tremens; brief mania a potu with suicidal and homicidal

impulses, July, 1898. Admitted to Colney Hatch, September 7, 1900, five weeks after sudden onset of acute multiple neuritis. Mental confusion, defective ideas as to time and place, loss of memory for recent impressions, delusion of recent confinement, and illusions as to identity of persons around her.

Complete paralysis of legs, with complete anæsthesia and analgesia, wasting of muscles and loss of reaction to faradism, and foot-drop; trophic blisters on heel and malleolus. Wasting of upper limb muscles, with marked weakness, especially of extensors; wrist-drop; diminution of faradic excitability; slight impairment of cutaneous sensation on forearms and hands without analgesia. Cutaneous sensation not perceptibly impaired on trunk, neck, and face. Weakness of muscles of neck and trunk. Partial right sixth palsy, with squint; double facial weakness, with defective articulation; tremor of lips and tongue; weakness of muscles of mastication; dysphagia; partial aphonia. General muscular tenderness to pressure, especially of limbs and abdomen; passive and active movements painful. Acute tenderness of limb nerves. Vision and hearing good; optic fundus normal; pupils reacted well to light and accommodation. Knee-jerks and plantar reflexes abolished; no upper limb jerks; abdominal reflex present. Partial paralysis of diaphragm. No paralysis of sphincters.

Dyspnœa and orthopnæa; respiration rate 26. Pulse 120-170, feeble, slightly irregular. Progressive cardiac dilatation, cyanosis, and hypostatic congestion of lungs. The comparatively slight paralysis of diaphragm did not appear sufficient to account for the rapid cardiac failure. No vomiting. No albuminuria. Constipation. No pigmentation of skin. No suspicion of arsenical poisoning. Patient was conscious up to the time of death, which occurred September 15, eight days after admission to asylum, or six weeks after onset of illness.

Autopsy.

Rigor mortis commencing. Slight excess of fluid in head. Dura mater normal. Very slight pia-arachnoid milkiness over frontal and parietal regions; no adhesion. No appreciable atrophy of convolutions. Brain 42 ozs., fairly well convoluted. No focal lesion. Basal vessels healthy. Heart 8 ozs., pale and greasy; Marchi sections showed slight fatty degeneration in places. No valvular lesion. Blood from jugulars fluid, of a dark laky colour,

contained quantities of *choline*. Lungs normal, save for slight hypostatic congestion of bases. Slight fatty cirrhosis of liver. Kidneys 7 ozs. each, cortex not diminished, capsules not thickened, slightly adherent in places, slight fatty change in renal epithelium. Mucous membrane of stomach vascular and congested, with patches of chronic inflammation and fibrosis. Intestines and other organs healthy.

Microscopical Appearances.

Peripheral Nerves.—No naked-eye changes. Small cutaneous branch to heel, anterior and posterior tibials, ulnar, musculo-spiral and median, examined by Marchi's method, showed intense acute degeneration of nearly all the fibres, with multiplication of their neurilemma nuclei. Both vagi affected, nearly half the fibres giving Marchi reaction. Left phrenic contained a few degenerated fibres. Tibials showed very slight interstitial proliferation commencing in places; none in the other nerves. No vascular or inflammatory changes.

Muscles.—Thenar muscles, triceps, and diaphragm (Marchi) showed acute fatty degeneration of many fibres, with proliferation of their sheath nuclei. Transverse striation preserved. No interstitial overgrowth. Soleus showed rather less fatty change, but some impairment of striation, and a very slight interstitial increase. No naked-eye change.

Vessels of spinal cord congested, otherwise quite normal. No neuroglial, meningeal, or other non-nervous changes.

Anterior horn cells of lumbo-sacral and cervical enlargements (Nissl) show acute changes. Severe chromatolysis commencing in the centre of the cell, and thence involving the whole cell body, with slight swelling and rounding of cell, and atrophy of dendrites. Nucleus swollen, pale, and displaced to the periphery, often bulging out from the side of the cell, though sometimes flattened against it. Nucleolus and membrane stain well, and usually appear normal; the membrane, however, in a few is granular and crumpled in association with extreme nuclear displacement. Actual loss of the nucleus has been searched for in vain; but rupture seems imminent in a few. Some excess of the normal yellow pigment. Nerve cells not invaded by glia cells, or leucocytes. A considerable number of cells of the anterior median group are normal, showing abundance of large stainable masses; these cells are believed to supply the spinal muscles. But all the cells of the other groups, supplying limb muscles are affected

in the manner described; none of these present even an approximately normal appearance. Those of the upper cervical and the dorsal regions are less affected than those of the lumbar and cervical enlargements. Marked changes of the same type are seen in the nuclei of the vagus, hypoglossal and sixth nerves, and the formatio reticularis, in the medulla. The cells of *Clarke's columns*, and also most of the other posterior cornual cells, are normal. The cells of the lumbo-sacral and lower cervical *posterior root ganglia* show similar lesions, very nearly one third of their number showing marked eccentricity of the nucleus, with chromatolysis.

There is degeneration of a very few fibres in the lumbo-sacral anterior and posterior roots.

Posterior columns (Marchi). Extensive degeneration of *exogenous* (posterior root) fibres, visible to naked eye in lumbar sections. No degeneration of cornu-commissural zones at any level, or of Flechsig's central oval area in the lumbar region; these situations are occupied by endogenous fibres; their integrity accords with the normal appearance of the posterior horn cells. Marked degeneration of root fibres in the root-zones, especially at limb levels. In the cervical region, there is much degeneration of the long fibres from lumbo-sacral roots, seen in the neighbourhood of the posterior median septum. Degeneration in funiculus gracilis and cuneatus.

Cerebellar tracts and *restiform bodies* not affected.

Slight degeneration in white matter of *cerebellum*, especially vermis.

Moderate degeneration of *pyramidal tracts*, through their whole extent in the cord, medulla, pons, crura, and internal capsules. In the *anterior limb of the capsule*, more degeneration than in the motor portion; numerous fibres giving Marchi reaction can be traced downwards, backwards, and inwards, into the gray matter of the thalamus.

Cerebral cortex.—Top of each ascending frontal gyrus (Nissl). Some of the Betz cells are normal; but most of them show a central and basal chromatolysis, with nuclear eccentricity, analogous to the anterior horn cell change, and of the kind described in notes of cortex of Case 2, in which the condition is more marked. Apart from slight fatty or pigmentary change, I have searched in vain for changes in the cortical blood-vessels. Marchi-Pal sections show a slight atrophy of *tangential fibres* in places. Marchi sections show a few degenerated fibres in the white matter of the motor convolutions.

CASE 2.—*Sub-acute alcoholic delirium, following fracture of femur, and fatal after ten weeks duration. Advanced fibrotic atrophy of tibial nerves. Vascular degeneration, slight in cortex, but severe in nerves, cord, medulla, and pons, with thromboses and hæmorrhages. Spinal ganglion cell changes and posterior column degeneration. Anterior cornual cell lesion. Degeneration of Clarke's cells and direct cerebellar tracts. Cortical cell lesions, and pyramidal and corticothalamic fibre degeneration.*

C. B., Italian, aged 49, female, married twenty-two years, no children. History of at least eight months excessive indulgence in white wine, brandy and gin; no beer. Had had several attacks of "nerves" (? delirium tremens). On January 26, 1901, fell downstairs while drunk, fracturing neck of left femur; no loss of consciousness. Forty-eight hours afterwards, she developed "delirium tremens," and lay in a state of constant muttering, with hallucinations, seeing cats, dogs, and other imaginary animals, and feeling them bite her; sleeplessness; refusal of solid food; constant craving for alcohol; passed urine and motions under her. Was treated in hospital and in workhouse infirmary, and from the latter was brought to Colney Hatch, on March 2.

On admission to asylum:—Poorly nourished, helpless and bed-ridden. Perpetually tossing about and throwing off the bed-clothes. No proper sleep. Much incoherent muttering. Paid no attention to questions, or to what went on around her. Once or twice recognised her husband, and asked him for brandy. Hallucinations very persistent—chiefly visual, occasionally pleasant or ludicrous. Repeatedly refused nourishment, and had to be fed by nurse. Action of bladder and bowels always involuntary. Though unable to raise herself in bed, she showed considerable power of resistance to examination; marked rigidity of arms. Elbows, wrists, and knees always flexed. Much coarse tremor of tongue, neck muscles, arms and hands. Legs almost completely paralysed. All muscles much wasted. Upper limb muscles re-acted fairly well to faradism, except triceps, which only responded to strong current. Quadriceps, calf muscles, and tibialis anticus, of both sides, scarcely re-acted to strong faradism. Patient objected to strong current applied to arms, but not to legs. Cutaneous sensation could not be satisfactorily tested owing to mental state; no apparent pains or tenderness. Knee-jerks absent, plantar reflexes lively. Pupils equal, of moderate size, re-action to light sluggish. Accommodation doubtful, owing to mental state and

almost complete defect of attention. Ophthalmoscopic examination unsatisfactory, owing to resistance; no obvious change in discs. Pulse 130, small, compressible, regular. Cardiac sounds weak; otherwise nothing abnormal noted in examination of chest or abdomen. Urine (by catheter) of fair quantity, clear, acid, sp. gr. 1025, albumen in readily recognisable trace. Never any vomiting, or urinous odour of breath. Temperature normal or subnormal, with occasional rise to 99° or 100°.

March 28. Small trophic blisters over right shin and left knee.

March 31. Slight diarrhœa (one day).

April 3. Absolutely "lost" and unresponsive, muttering incoherently. Coarse tremor of arms, more marked, with short series of clonic movements, of 25 vibrations in 5 seconds.

Respiration rose to 44, pulse became almost imperceptible. She lay in a moribund state several days, and died April 6, ten weeks after the accident, the delirium having persisted throughout.

Autopsy.

Rigor mortis present. Emaciated. Healing sores on legs. Bony union of fracture.

Calvaria and dura normal. Excess of subdural and subarachnoid fluid. Slight opacity and thickening of pia-arachnoid over parietal and frontal lobes. Congestion of meningeal veins. Some rounding of convolutions and widening of sulci. Pia stripped fairly readily without tearing cortex. Cerebral vessels apparently healthy.

Lungs. Cavity in right lung, size of an olive; firm localised pleural adhesions at this spot. Some hypostatic congestion of bases.

Heart pale and flabby; left ventricle contracted and empty; whitish clot in right side and in aortic arch; slight atheroma above valves. No valvular lesion. Muscle substance from left ventricle (Marchi, hæmatoxylin) showed intense universal acute fatty change in all the fibres, but scarcely any impairment of transverse striation, and no nuclear proliferation.

Liver deformed, globular, pale; slight nodulation of under surface with thickening of capsule. Marchi and hæmatoxylin sections show a moderate fine cirrhosis of portal distribution, fairly well marked fatty infiltration, and slight fatty degeneration in liver cells; no cloudy change.

Kidneys macroscopically normal on section; very slight adhesion of capsule in places. Marchi and hæmatoxylin-eosin

sections show a good deal of fatty change in the renal epithelium, especially of the medulla; slight thickening of intima and media of some of the arteries; slight interstitial overgrowth beneath capsule.

Peritoneum normal. Stomach apparently normal. Some congestion of jejunum in places; no ulceration. Spleen normal. Chronic thickening of bladder. Uterus and ovaries shrunken.

Brain weighed 40 ozs., heart 10, right lung 13, left 15, liver 36, spleen 2½, and kidneys 4 ozs. each.

Microscopical Examination of Nervous System.

Peripheral Nerves.—Left Posterior Tibial, at ankle (Marchi, hæmatoxylin-eosin), shows very great fibrosis; the nerve bundles are almost entirely converted into dense fibrous tissue permeated by numerous small vessels. There are only a few nerve-fibres left here and there, and many of these give the Marchi reaction. There is thickening of the media and intima of many of the arteries (atheroma); some contain clots, in which focal collections of leucocytes are seen, and organisation appears to be commencing.

Left anterior tibial, in middle of leg, is in a similar condition. The anterior tibial artery shows thickening of the inner coat.

The arm nerves show much less change. Many of the fibres of the left *ulnar* (at wrist) show a cloudy granular appearance of the myelin, without segmentation; a few blackened droplets, but no definite Marchi reaction. No nuclear proliferation, or interstitial overgrowth. The ulnar artery is atheromatous, and contains a small clot commencing to organise. A large clot is also seen in a big vein lying next to it. A small artery in the nerve itself shows general thickening, and contains a clot.

Left musculo-spiral (in lower third of arm) shows slight recent degeneration. Some multiplication of neurilemmal and endoneurial nuclei, with commencing interstitial fibrosis.

Left median (at elbow) shows a few fibres giving definite Marchi reaction of degeneration. There is less nuclear proliferation than in the musculo-spiral. The median at the wrist presents the same appearances as at the elbow.

A few fibres giving the Marchi reaction are seen in the *optic nerves and tracts*.

Anterior horn cells of the cord.—These are much more affected in the lumbar enlargement than in the dorsal and cervical regions. They present the same extreme degrees of central chromatolysis

and nuclear eccentricity that were seen in Case 1. At all levels, the anterior median group supplying muscles of the spine, seems to be nearly as much affected as the others. There is marked general excess of yellow pigment, which, in the lumbar cells, shows a distinct predilection for the periphery of the cell and the bases of the dendrites; in the cervical enlargement, it is more commonly seen as a mass in the midst of the cell. The chromatolysis is seen in many of the cervical cells, but not so marked as in the lumbar region; truly normal examples, however, are scarce.

Cells of posterior horns.—Nearly all these show a similar type of chromatolysis.

The same kind of change is seen in the cells of *Clarke's columns*; none of these appear normal, the great majority are entirely devoid of Nissl-bodies.

In the examination of the cells of the *posterior root ganglia*, the Nissl method was supplemented by Heidenhain's iron-hæmatoxylin. Nuclear eccentricity occurs in only a very few of them; there are no very marked chromolytic changes; there is an excess of pigment, often at the periphery of the cell. In three or four cells in each section, the nucleolus is swollen and intensely stained, while the nucleus is reduced in size, preserves its uniform oval outline, and stains somewhat deeper than normally.

Purkinje's cells of the *cerebellum* show no definite changes. There is slight fibre degeneration in the white matter of the vermis and lateral lobe.

Nissl-sections from several levels of the medulla and pons show in a number of cells of the cranial nerve nuclei, changes similar to those observed in the lumbar anterior horn cells, but more severe.

Cerebral cortex.—Upper parts of ascending frontal and parietal gyri of both sides (formol-paraffin-Nissl). None of the Betz-cells are normal. Their large masses of stainable substance are broken up into a fine powder or granular debris; the parts of the cell thus affected are distinctly paler than they should be. The alteration affects chiefly the central parts of the cell, but may extend to the periphery, in which case the basal part is more affected than the other peripheral regions. Some more or less large masses of stainable substance often persist at the sides and apex of the cell, and on the dendrites, especially the apical process. In association with a chromatolysis of this kind (which, in some few of the cells, is complete) there is observed a displacement of the nucleus to the side or to the upper extremity of the cell. The

nucleus may be swollen and bulging, or may be flattened. The nucleus remains pale, its membrane and nucleolus stain with normal intensity, and the former may be granular. Many of the medium-sized pyramids are beset with glia cells. There is no disarrangement of the cell layers and columns.

Sections prepared by Busch's modification of Marchi's method show numerous degenerated fibres in the white matter of the motor convolutions, and still more in the visual area (right calcarine fissure). There is slight pigmentary change in the minute vessels of the cortex, slight thickening of smaller arteries, and some dilatation of perivascular spaces, but no perivascular infiltration. The vascular changes are trivial compared with those in the cord.

A few degenerated fibres are seen in the part of the *Corpus Callosum* opposite the motor areas.

In the *anterior limb of the Internal Capsule*, numerous degenerated fibres can be seen running downwards, backwards, and inwards, into the gray matter of the thalamus, as in the other cases.

There is considerable degeneration in the *Pyramidal Tracts*, from the internal capsule downwards to the sacral region.

The *Direct Cerebellar Tracts* and *Restiform Bodies* are extensively degenerated.

In the whole cross section of the *Posterior Columns* of the cord there is considerable diffuse degeneration, most evident in the cervical region, and diminishing as the cord is traced downwards. It is also seen in the funiculus gracilis and cuneatus in the medulla. The cornu-commissural zones have not escaped, so that the endogenous fibres appear to be implicated. But the exogenous fibres are more extensively affected; and this is more evident in the lumbar region. In the cervical part the degeneration is most marked in the posterior root fibres, in the root zones, and in Goll's columns near the middle line (situation of long fibres from lumbo-sacral roots). In the upper dorsal levels it is mostly in Goll's columns. In the mid-dorsal region it is more diffuse. At the twelfth dorsal segment it is most marked in the middle of each posterior column; there is less degeneration near the gray matter and median septum. There is not much in the lumbo-sacral region; what there is is chiefly in the root zones. Thus the lesion of the exogenous fibres (derived from posterior roots) appears to preponderate over that of the endogenous fibres.

Nearly all the blood-vessels of the cord are irregularly thickened and tortuous. There is general vascular engorgement.

There are a number of small hæmorrhages in the spinal gray matter; I have not observed any in the white columns. They occur anywhere in the anterior or posterior horn, and are most numerous in the lowest cervical segments; a few are seen in the upper dorsal region, but none lower than this. In sections stained by Van Gieson's method, there is also seen a slight increase of interstitial tissue in Goll's columns in the cervical region, and also in the crossed pyramidal tracts. Amyloid bodies are numerous in the membranes, and in the periphery of the white matter. Thrombi are seen in a few of the larger vessels of the medulla and pons.

Voluntary Muscles (Marchi, hæmatoxylin). Those of the hypothenar eminence show an acute fatty change, affecting different individual fibres selectively, and accompanied by some proliferation of the nuclei of their sheaths. There is no marked interstitial increase, and no appreciable loss of transverse striation, except in a few of the fattiest fibres. A similar condition is seen in the triceps. In the tibialis anticus, the fatty degeneration is less, there is some impairment of striation in places, and a slight interstitial overgrowth. There is thickening of the coats of the small arteries in this muscle.

CASE 3.—*Acute alcoholic mental confusion of "polyneuritic" type. Chronic neuritis. Tuberculosis of lungs. Cortical cell changes. Degeneration of fronto-thalamic fibres, pyramidal tracts, and posterior columns.*

C. K., married woman, aged 45, dressmaker; addicted to beer and spirits several years. Admitted to Colney Hatch, Sept. 8, 1900; duration of mental disorder then stated to have been one week. Short previous attack 3 years ago (not in asylum). On admission, she was emaciated and feeble, and scarcely able to stand; had been refusing her food. Depressed and apathetic; gave irrelevant answers to questions. Had no idea where she was, or how long she had been there. Often thought she was at home; talked of selling her furniture, which she thought she saw in the bare half-padded room where she lay. Once she said, "This is the Hearts of Union Oak." She thought the nurse was her sister. She gave accounts of imaginary journeys she had made "yesterday" or "to-day":—she had been to church, and on her way home slipped and fell, hurting her knee; another time, she had been to Regent Street, to make designs for wall-papers (this she had never done). Thought she was required to get up and do dressmaking jobs, and protested she was unable.

Continually asking all who went near her for beer, gin or brandy; but if asked whether she liked beer she would profess disgust. Very inattentive to questions, or to what went on around. Talkative, mumbling incoherently. Constantly tossing about; had to be placed in padded room to prevent her injuring herself falling out of bed. Passed urine and motions under her.

Fine tremor of tongue, facial muscles and hands. Slight facial weakness, more on right side. All muscles of upper limbs wasted, especially triceps, interossei, and thenar and hypothenar muscles; wrist drop; faradic reaction almost abolished in deltoids, triceps, and small thumb muscles. Muscles of lower limbs flabby and wasted; marked general impairment of faradic excitability. Muscular tenderness, especially of calves, triceps and small thumb muscles. Tenderness of posterior tibial nerves. Knee-jerks absent; plantar reflexes sluggish and feeble. Cutaneous sensation could not be satisfactorily tested, owing to mental state, but there was at any rate no marked analgesia to pin-prick. Pupil reactions normal. Optic discs normal. Pulse 120, regular, feeble. Respiration 30, some cough, signs of consolidation over part of right apex. Evening rise of temperature to 100° or 101°. Became more exhausted and dyspnœic, and had several syncopal attacks, in one of which she died, six days after admission (September 13); conscious up to time of death.

Autopsy.

Rigor mortis present. Skull-cap and dura normal; very slight milkiness of pia-arachnoid over parietal and frontal convexity; no adhesion of membranes; no excess of fluid; practically no wasting of convolutions; brain weighed 42½ ozs.; ependyma of ventricles smooth; no focal lesions; basal vessels healthy. Small amount of caseous tubercle at apex of each lung, some hypostatic congestion of bases. Heart, 7½ ozs.; cardiac muscle pale and friable; some dilatation of right side; valves and aorta healthy. Liver, 42 ozs., soft, fatty, some passive congestion. Kidneys, 5 ozs. each, normal to naked eye; microscopically, very slight interstitial increase. Stomach, intestines, spleen, and pelvic organs, normal.

Microscopical.

Some of the nerves were accidentally spoiled; but the posterior tibial shows a marked fibrotic atrophy, the number of nerve-fibres left being very small; some of these give the Marchi reaction. A few fibres of the median nerve give the Marchi reaction, but otherwise the nerve appears normal.

The anterior horn cells are much less changed than in the other cases; however, there is a general diminution in size of Nissl-granules, and in a fair number of cells there is definite central chromatolysis, with more or less displacement of the nucleus; there is marked excess of pigment. Chromolytic changes are more marked in Clarke's cells. The cranial nerve-cells in the medulla and pons are severely affected with change of the same type as in Cases 1 and 2; extreme displacement of the nucleus, with flattening and crumpling of the membrane. The large cells of the reticular formation are affected in like manner. No definite changes have been made out in Purkinje's cells of the cerebellar cortex; Busch sections of the vermis show numerous degenerated fibres in the white matter; the lateral lobe shows fewer.

Busch's method shows numerous degenerated fibres in the pyramidal system at all levels, in the internal capsule, crura, pons, medulla, and cord; the last was examined at nine different levels. In the anterior limb of the capsule, there are large numbers of degenerated fibres seen running backwards into the thalamus. There is some degeneration of the direct cerebellar tracts.

Of all the columns of the cord, the posterior columns show the most degeneration. In the cervical region it is most marked in Goll's columns bordering each side of the median line, and also in the root zones; there is a slight diffuse degeneration in Burdach's column; the cornu-commissural zones appear to be free. In the dorsal region the degeneration is somewhat diffuse, but is most marked in Goll's columns and in the more posterior parts. In the lumbar region the central oval area of Flechsig escapes, though all around it there is a good deal of degeneration; there is marked degeneration in the posterior root zones, of fibres which have just entered the cord; the cornu-commissural zones are apparently free from degeneration. The lesion is, therefore, mainly an affection of exogenous fibres, as in Cases 1 and 2.

There are no appreciable vascular changes in the brain and cord.

The appearance of the cortex of the paracentral lobule of each side is scarcely distinguishable from that seen in Case 2. There is the same type of Betz-cell change as in the other two cases; none of these giants are normal. There is some excess of satellites about the pyramidal cells, and a slight proliferation of glia nuclei in the deeper layers. There is scarcely any abnormality in the small vessels, and no cell proliferation in their sheaths.

The cardiac muscle shows a distinct nuclear proliferation in the interstices between the fibres.

The diagnosis of neuritis in these cases is established by the microscopical appearances. All three patients were alcoholics. The form of mental disorder in each case is consistent with the view that it and the neuritis were related to the alcoholic condition. Case 1 is an example of an acute polyneuritis of cranial and spinal nerves; in the other two there is found a more chronic form. In the first case there is practically no interstitial or vascular change anywhere in the nervous system; in the third also there is very little. But in the second, vascular changes are severe in the nerves, cord and medulla, and slight in the cerebrum. In Cases 2 and 3, there is advanced fibrotic atrophy of some of the nerves. The table here given may be helpful in presenting concisely the degree and distribution of the various changes. A minus sign signifies "normal," or "no appreciable alteration"; one or more plus signs indicate the presence and degree of change.

	Case 1.	Case 2.	Case 3.
Acute degeneration in nerves	++++	—	—
Fibrosis of tibials	—	++++	++++
Vascular changes in nerves	—	++++	+
,, ,, cord	—	++++	—
Anterior cornual cells:			
Lumbo-sacral	++++	+++	++
Dorsal	++	++	+
Cervical	++++	++	+
Spinal ganglion cells	++++	+	(not examined)
Exogenous fibres of posterior columns:			
Lumbar	++++	++	+
Dorsal	++	++	+
Cervical	+++	+++	+
Posterior horn cells	--	++	—
Endogenous fibres of post. columns:			
Lumbar	-	+	—
Dorsal	—	++	—
Cervical	—	++	—
Cells of Clarke's columns	—	++++	+
Direct cerebellar tracts	—	++++	+
Cells of cranial nerves	++++	+++	+++
Betz cells of cortex	+++	++++	++++
Pyramidal tracts	++	+++	+
Fronto-thalamic fibres	++++	+++	++++

We may proceed to consider the significance of the changes in the brain and cord, in relation to the general

nature of alcoholic paralysis, and in relation to the peripheral neuritis. The whole question is conveniently approached by some preliminary consideration of certain features of the peripheral nerve lesions which have an important bearing on the interpretation of the central changes.

Few pathologists now hold that alcoholic neuritis consists in an inflammatory affection of the nerves. It is essentially a degeneration of the nerve-fibres, as is evident from the study of acute cases, like Case 1, or those reported by H. H. Tooth and by Sidney Martin. In such cases, the appearances resemble those seen in early stages of Wallerian degeneration after nerve section. There is severe acute degeneration of the fibres, in spite of complete (or almost complete) absence of change in the sheaths, connective tissue and vessels. Indeed, the more severe the degeneration, the more striking is the absence of vascular and interstitial changes. These cannot, therefore, be the cause of the fibre degeneration; in those cases in which such changes occur, we must regard them as secondary. For proliferation of neurilemma nuclei and connective tissue-cells, diapedesis of leucocytes, and formation of new fibrous tissue, all appear successively in Wallerian degeneration, and follow as the result of the injury to the nerve-fibres. We may therefore justifiably infer an analogous causation for the similar interstitial changes in sub-acute and chronic neuritis. So far simply as the nerves alone are concerned, the fibre degeneration is the primary element of the neuritic process.

Vascular and interstitial causes of the degeneration being excluded, at least in many acute cases, we might be tempted to ascribe it simply to direct local toxic action on the nerve fibres themselves. But the selective nature of the process is not easily explained as a selection of fibres as such. Apart from the apparent histological similarity of all peripheral fibres, we find that in the various forms of toxic neuritis certain groups of fibres are selected by one poison, and others by another. The selection therefore, cannot be due to local and anatomical factors, since they would be more or less the same for all forms. Though alcoholic neuritis is usually of the "multiple" variety, yet some nerves are

affected more than others. Thus, the motor and sensory paralysis is more marked in the limbs than in the trunk, and more marked in most cases in the distal parts of the limbs than in the proximal parts. This is not adequately explained as the mere result of defective circulation in the extremities, impairing the nutrition of their nerves and so rendering them more vulnerable. Nor is the marked affection of the long nerves, such as the limb nerves, phrenics and vagi, adequately explained by the fact that their fibres have a greater extent of surface exposed to toxines in the blood. For it is not universally true that the longest fibres are the most affected. Thus, one occasionally meets with cases in which the arms are more affected than the legs, or in which the deltoids and glutei are the most affected muscles, as in a case I have in Colney Hatch, which was referred to by Dr. Mott, in his Croonian Lectures. And, in quite analogous fashion, I have more than once found the sensory affection of the extremities less marked distally than proximally, sensation being less impaired on the feet than on the legs.

Moreover, the extensor muscles of the limbs are usually more paralysed than the flexors. This fact cannot be explained by blood stagnation or the length of nerves; nor can it be attributed to stress. The extensors of the legs are perhaps more used than the flexors, as in maintaining the erect posture and in walking. But in the upper extremities the reverse condition holds, for most persons use the flexors of the arms more than the extensors, and the biceps distinctly more than the triceps. Strain, or overwork of certain muscles, may modify distribution of paralysis in certain individuals of special occupations, but cannot account for the typical selective distribution in ordinary cases.

The essential feature of the muscle change is a fatty degeneration, affecting individual fibres somewhat selectively, and independent of interstitial fibrosis. The cross striation is usually unimpaired by the fatty change. The interstitial fibrosis, commonly described as the characteristic muscle change in neuritis, appears to be simply an end-product. The fatty change has not received sufficient recognition. It seems probable that the muscle degeneration is partly the

result of direct toxic action on the muscle substance, and not simply of damage to the nerve supply. If so, the difference of degree of paralysis of extensor and flexor muscles may be partly determined by the physiological differences normally existing between their respective contractile tissues—differences such as those illustrated by Bierfreund's experiments. In whatever way the muscle degeneration is brought about, the limb nerves may suffer more severely than they otherwise would, because they lie in great part of their course in the midst of a large mass of degenerating muscle, and hence are bathed in lymph loaded with deleterious products; the nerves and muscles may thus to some extent be involved in a vicious circle.

But none of the various anatomical and physiological factors I have indicated can fully account for the distribution of any form of toxic neuritis. The distribution varies in type according to the particular poison or toxine at work. There is obviously a far more important principle of selection, of a very special kind, consisting in a particular preference of the individual poison for particular groups of nerve elements. Only in this way can we explain the various localised forms of lead palsy, or the ocular and vagus paralyses in diphtheria. Apart from neuritis, the acute intoxications afford many instances of the characteristic selection of different nervous structures by different poisons. The phenomena of idiosyncrasy show that the selection is characteristic, not only for the individual poison, but also for the individual patient. Susceptibility varies largely according to hereditary and developmental factors, and also according to acquired characters, as is shown in the establishment of tolerance and in other ways.

Such differences of susceptibility can only depend on inherent qualities of the nervous elements. We can scarcely imagine, however, that certain nerve-fibres are picked out by a particular poison on account of any qualities they may possess as mere fibres. For example, we cannot well suppose that lead selects the *fibres* supplying a particular complex group of muscles, and avoids fibres in the immediate neighbourhood going to other muscles or to the skin; for they are

all so similar and similarly situated. The neurone theory, however, affords an intelligible explanation. All the fibres are exposed to the action of the poison or toxine; but particular fibres succumb to it, because their axis cylinders are simply parts of specially susceptible *neurones*, which are subjected, over the whole extent of their cell-bodies and processes, to the all-pervading influence of the poison in the blood. The peculiarities which constitute the basis for special selection by poisons must surely belong to the individuality of the neurone as a whole.[1]

If there should appear to be a selection of the long fibres, it would readily resolve itself into a selection of neurones. For the longer the fibre the more should we expect the trophic influence of the poisoned cell to become inadequate for the maintenance of the remotest parts. If there were simply a selection of fibres as such, we should expect to find more degeneration in the roots and highest parts of the nerves than there is; usually there is little or none. But on the theory of a neuronal affection the facts are explicable: as the poisoned neurone is progressively damaged, the parts which suffer most are those furthest removed from the trophic influence of the cell.

Though local conditions may have an influence (as in diphtheritic paralysis of the palate), yet in all forms of toxic neuritis the distribution forcibly suggests a selective affection of whole neurones. The changes in the brain and cord further support this view. We may pass on to consider, in relation to this question, the changes in the nerve-cells.

[1] It has been thought by some that the validity of the neurone theory, as applied to peripheral nerves, is impugned by the observations of Vulpian, R. Kennedy, and others, on regeneration of nerve-fibres. They have shown that in the distal portion of a divided nerve, though still separated from its central connections, new fibres are developed from the sheaths of the old ones. The question thus arises, whether the peripheral axis cylinder is indeed a part of the spinal cell, as we have been wont to believe. But, at any rate, the fibre and cell are intimately associated both structurally and functionally, and injury to either reacts upon the other. Without committing ourselves on this question, we may yet conveniently retain the word "neurone" as a descriptive term, to embrace the nerve-cell and its processes, with the peripheral fibre in its whole length. For the purpose of the present argument I may, without prejudice, use the word in this sense. The different parts of such a neurone may possess a limited local autonomy, but the cell is paramount, and the whole neurone comports itself for the most part as an individual.

The changes in the anterior horn cells have been described by Achard and Soupault, Ballet and Dutil, Dejerine and Thomas, Soukhanoff, Marinesco, Heilbronner, Larkin and Jelliffe, Mott, Wright and Orange. They are well exemplified in my cases. An analogous lesion is seen in the spinal ganglion cells of Case 1 (*cf.* Soukhanoff: Wright and Orange); and a change of the same type affects the Betz cells of the cortex in each case, and also many groups of cells in the pons and medulla. In all these different situations the cell changes conform to the same type. The Nissl-bodies, or large masses of stainable substance, are broken up and reduced to a fine dust, more or less uniformly distributed in the affected parts of the cell, which thus appear faintly and diffusely stained in Nissl-sections. The process of disintegration begins in the middle of the cell, near the nucleus, and thence spreads outwards in every direction, involving the whole cell-body progressively. The last stainable masses to disappear are those on the roots of the dendrites and a few attenuated clumps around the margin of the cell. Simultaneously with this process there occurs a displacement of the nucleus to the periphery.

This form of alteration closely resembles that which section of a nerve trunk produces in the cells of origin of the nerve. It has been called "reaction at a distance," "secondary cell change," or "axonal reaction." Marinesco and others, arguing by analogy, interpret the cell alteration in neuritis as a secondary change set up by the damage to the axis cylinder in the neuritic process.

The objection to this interpretation is, that the cell change in question does not necessarily signify preceding damage to the axon.

For numerous observations show that the same change may occur under conditions in which there is no axis cylinder lesion to produce it. Thus it is seen in the motor cells of the cord (and also in Clarke's cells) after section of posterior roots (Warrington). It is found widely distributed in the nervous system in certain acute diseases, when there are no recognisable axis cylinder lesions, and when the rapidly fatal result renders it improbable that the cells have been so

affected. I may refer to the observations of Ewing and Bonhoeffer on delirium tremens, of Colucci and Worcester on Landry's paralysis, and of C. Bolton on the cells of the vagus nucleus in acute fatal diphtheria. The occurrence of this cell change in acute disease of any kind is very significant, and in none more so than in Landry's paralysis. The pathology of this affection is little understood; but whether it be a separate entity, or only a rapid form of polyneuritis, the significance of the observation is the same. The virulent character of the disease, its strong motor bias, and the appearance of its cell lesions before appreciable fibre degeneration (Worcester) speak strongly against a peripheral initiation. If, however, the disease is identical with polyneuritis, as the researches of Ross and Bury appear to indicate, then their differences become simply differences of degree, and further ground is afforded for the belief that "polyneuritis" depends upon an affection of whole neurones.

The so-called "axonal" type differs from the peripheral chromatolysis seen in the primary lesions of the cell in many acute poisonings, or after artificial elevation of body-temperature, or ligature of the aorta. But such overwhelming experimental injury can scarcely represent the appearances in all the morbid conditions in which the cell is directly affected. It would appear futile to attempt to draw a hard and fast line between primary and secondary affections of the cell; for the neurone being a living organism, there must be a process of interaction constantly going on between all its parts.

Many poisons and toxines, which, if present in a large dose, cause a rapidly fatal result, with a "primary" type of cell change, may, on the other hand, if absorbed in smaller quantities over a sufficient period, apparently set up a neuritis, with a "secondary" type of cell change. But in each case the toxic substance is everywhere distributed in the blood, and is brought to every part of the neurone. It would seem that repeated small doses partially impair the vitality of the whole neurone, leading first to decay of its remotest parts, which then reacts on the cell and so introduces a "secondary" element into the cell affection.

But between the two extreme types, there may be any number of intermediate grades, varying according to acuteness or chronicity of intoxication, or according to differences of resistance of the various portions of the neurone. Though the nerve degeneration in neuritis probably reacts deleteriously on the cells, the changes in the neurones do not begin in their processes. This appears to be clearly demonstrated by the appearances in the sensory neurones.

The spinal ganglion cells show changes of similar type to those in the anterior cornual cells; they are especially severe and conspicuous in the acute Case 1. In addition, there is extensive acute degeneration of their central prolongations in the posterior columns of the cord. In the acute case, the posterior column degeneration appears to affect exclusively the *exogenous* fibres, which enter from the posterior roots, and which, therefore, are processes of spinal ganglion cells. The degeneration is especially severe in those exogenous fibres which are processes of cells in the lower cervical and the lumbo-sacral ganglia, corresponding to the upper and lower extremities respectively. In this case, the posterior column degeneration does not affect the endogenous fibres, or processes of cells in the gray matter of the cord; such fibres are mainly situated in the cornu-commissural zones, and, in the lumbar region, in Flechsig's central oval area. These are normal.

The conspicuously selective affection of the exogenous fibres, especially those from arm and leg roots, clearly shows that the cord lesion represents a degeneration of those same sensory neurones whose peripheral processes are degenerated in the nerves, and whose cells show changes in the corresponding root ganglia. At the same time, very few of their root fibres outside the cord give the Marchi reaction of degeneration; the parts nearest the trophic cells are the least affected.

The view which accords best with these appearances is that which regards the central and peripheral fibre degenerations as simultaneous manifestations of a single disorder of the whole sensory neurone. And, indeed, no other

explanation seems admissible. For what conceivable alternatives have we?

I am not aware that it has even been suggested that the neuritis is secondary to the posterior column degeneration. Such a theory would not only lack evidence, but would appear to be negatived by the fact that section of posterior roots does not produce nerve degeneration. It is equally easy to dispose of the converse theory—that the cord lesion is originated by the nerve lesion. For after section of a nerve, or amputation of a limb, the Marchi method shows no degeneration in the posterior columns; there is only a very slow disuse atrophy. Thus the lesions of central and peripheral prolongations cannot stand to one another in any way in the relation of cause and effect, unless we at the same time postulate an impairment of the resistance of the whole neurone; in other words, a general affection of the neurone.

The only remaining alternative is that the cord lesion is a phenomenon entirely independent of the neuritis. But this would require us to believe that even in uncomplicated typical acute cases, the sensory neurones are damaged by two simultaneous processes, both of which, though quite distinct from one another, yet, by some curious coincidence, have a notable selective preference for the same group of neurones, and even for its particular sub-groups (those of the limbs). This is Heilbronner's view, though he gives no valid reason for such a disregard of the logical injunction against multiplication of causes. He bases his contention mainly on the appearances in the root fibres in his Marchi preparations. Those of the anterior as well as the posterior roots appeared to be degenerated within the cord, but not outside; the change was sharply marked off at the point where they entered or issued from the cord. He therefore thinks that the affection of root fibres within the cord is a separate lesion, *sui generis*. He admits that it cannot be attributed to a meningeal lesion at the point of entrance or exit; for, on the Wallerian principle, that would cause the anterior root fibres to degenerate outside the cord, away from their cells. Moreover, there is no evidence of such

lesion. The crux of the matter lies in the paradoxical appearances in these motor fibres, which gave the Marchi reaction of degeneration in the nerves and within the cord, but were normal in their intermediate parts situated in the roots. That their intermediate portions could remain normal under such circumstances seems incomprehensible, and quite at variance with all we know of their behaviour.

There would appear to be some fallacy in the observation. Heilbronner seems to realise this to some extent, and considers several possible fallacies ; but he overlooks the most probable, which is, that the anterior root fibres in the cord were not really degenerated, but gave the Marchi reaction because of *post-mortem* damage. If the roots are pulled upon in removing the cord from the body, the root fibres outside the cord are protected by their tough external sheath ; but their continuations within the cord have no such protection against stretching, and hence their myelin is damaged. Blackening in Marchi specimens under such circumstances is a familiar observation, and of no pathological import.

But that the degeneration of exogenous fibres is genuine is shown by its systematic distribution over the cross section of the posterior columns at different levels, the long lumbar fibres being degenerated even in the cervical region. Damage by stretching could only extend a short distance into the cord. Thus we can be sure that there is real degeneration of these fibres. But outside the cord they may be better able to preserve their myelin, as there they have primitive sheaths, and are nearer their cells.

By such a process of exclusion of alternatives we are reduced to our first hypothesis, viz., that of a general affection of the whole sensory neurone.

Moreover, the degeneration must begin in the neurone itself, for in many of the severest cases there is no meningeal, interstitial, or vascular change. Yet I would not be thought to undervalue the importance of vascular lesions. In Case 2 there is advanced vascular degeneration, and in the spinal cord there are numerous small hæmorrhages. Such lesions must inevitably cause damage of the nervous

elements. But the exogenous degeneration is more conspicuously selective, and even more intense, in the acute case without vascular lesions, than in the case with vascular lesions. There is, therefore, a selection of these neurones, independent of alteration in their structural environment.

The theory of a general affection of whole neurones is especially supported by severe acute cases, like Case 1; but in the less virulent cases, more opportunity is afforded for the modifying influence of differences in the constitution and environment of the two prolongations of the sensory neurone. They are probably not homologous, and in the peripheral process conduction of impulses is cellulipetal, while in the central it is cellulifugal. There is a more liberal blood-supply in the nerves than in the posterior columns; but blood stagnation in the extremities may render the peripheral process more vulnerable to toxic action, and it seems also more liable to poisoning by products of muscle degeneration. On the other hand, in some cases, the central process is more liable to damage from vascular lesions. The peripheral fibre has a primitive sheath, but the central has not; for this and other reasons, the central fibre has less capacity for repair, if its axon be broken. Waste substances are probably more rapidly removed from the nerves than from the cord; this is, at any rate, true of the products of myelin degeneration which give the Marchi reaction; hence allowance must be made for this fact, in the interpretation of Marchi preparations. And just as clinical experience shows that the neuritic condition admits of improvement, so the microscopical appearances in the nerve-cells and spinal roots show that the affection usually stops short of destruction of the neurone. Therefore, if the axon of either prolongation be only partially impaired, or be able to grow again, its myelin may be restored. In long-standing cases, the appearances may be modified by all these multifarious circumstances, especially if amelioration has taken place. But in acute cases, like Case 1, the morbid process reveals itself as a general affection of the whole neurone. Hence we find a more or less equal degeneration of the central and peripheral prolongations simultaneously, and also a cell change.

The fibre degeneration may perhaps be likened to gangrene of extremities arising in an old man as the result of general impairment of vitality. As this impairment may lead to a symmetrical gangrene of both feet, so the affection of the whole neurone may lead to degeneration of both its prolongations. But just as the gangrene does not necessarily involve the whole limb, so the proximal parts of the neurone may escape actual degeneration; though, as the proximal parts of the affected limb may be in a state of low vitality without actually becoming gangrenous, so it is possible that the myelin of those parts of the fibre nearest the trophic cell may be altered, though not to such an extent as to give the chemical test on which the Marchi reaction depends. Just as the gangrene further impairs the patient's originally feeble state, so the degeneration of the outlying parts of the neurone reacts upon the cell. Moreover in the same way that external injury may determine gangrene in a feeble patient, so unfavourable local conditions may precipitate the onset of degeneration in an already impaired neurone. Also as slight injury may determine gangrene in one or other foot, so any slight unfavourable difference of environment may determine degeneration in one or other prolongation, central or peripheral; so that in some cases (*cf.* Vierordt) the central prolongation of these neurones may be chiefly affected, and in others (*cf.* Marinesco) the peripheral prolongations. But in the same way that the gangrene would not have occurred in a healthy patient, so the fibre degeneration would not have occurred in a healthy neurone. To suppose that the fibre degeneration is the cause of the neurone affection, would be analogous to supposing that gangrene is the cause of senility. Just as many old men present the conditions favourable to the production of gangrene without actually developing it, so, too, many neurones show the characteristic cell change without fibre degeneration; this is seen in many of the cortical neurones (*e.g.* in Case 3). The analogy must not be pushed too far, however, for under appropriate conditions the degenerated fibre may be

restored, though a gangrenous limb can never grow again. Also, I would not be thought to imply that the toxic neuronal affection is actually a premature senility, though the marked excess of pigment in many cells resembles that seen in old age.

Posterior column degenerations in polyneuritis have been described by Vierordt, Korsakow, Kojewnikow, Pal, Biedekarken, Campbell, Soukhanoff, Heilbronner, Wright and Orange, Goldscheider and Moxter, and Marinesco. It seems usual for such lesions to be present; for I can find no record of any case in which the cord was examined by Marchi's method, in which it is stated that the posterior columns were free from degeneration. In Marinesco's case, there was degeneration mainly of endogenous fibres; but with this one exception, an analysis of all the above records shows that the degeneration affected chiefly the exogenous fibres, belonging to peripheral neurones. In my Case 1, the degeneration appears to affect the exogenous fibres exclusively. In Case 2, both systems are affected, but mainly the exogenous. In both cases, the fibres most affected are those derived from the roots connected with the arm and leg. In Case 3, the degeneration is slighter, mainly exogenous.

The occasional affection of the *endogenous* tracts of the cord is not surprising, as the disease evidently affects neurones of many different orders. In Case 2, the lesions of posterior cornual cells and the endogenous fibres in the posterior columns, and the lesions of Clarke's cells and the direct cerebellar tracts, may be partly due to vascular damage. In the light of Warrington's experiments, however, (*vide supra*), one might be tempted perhaps to explain them on van Gehuchten's principle of the reaction of the ganglion cells of a nervous chain upon one another; the secondary spinal afferent neurones might be thus affected because their peripheral stimuli are cut off by reason of the neuritis. But if so, the absence of changes in these secondary neurones in Case 1 is remarkable, unless their development was forestalled by the patient's early death. I am strongly inclined to think that their absence here, and their marked preponderance in

Marinesco's case, point rather to a primary element in the endogenous degenerations, determined by a special susceptibility of these neurones in certain patients.

The affection of the exogenous fibres commonly makes the posterior column degeneration approximate in distribution to that of tabes. This reminds us that cases of alcoholic paralysis have been described, in which ataxic symptoms have been prominent, sometimes overshadowing the neuritic symptoms proper. For such cases, the name "alcoholic pseudo-tabes" has been devised. It is not impossible that in rare instances there may be a difficulty of diagnosis. We may bear in mind that neuritis is typically associated with posterior column degeneration of more or less tabetic distribution, that neuritis may not be conspicuous in its late stages, and also that in true tabes there is often some neuritis as well. Argyll Robertson pupil, however, may probably be regarded as unknown in neuritis, apart from previous syphilis. It was not met with in twenty-eight cases of alcoholic neuritis in which I examined the pupils; nor did any of these exhibit the reverse condition, which Lauder Brunton describes as characteristic of alcoholic neuritis, viz., abolition of contraction to accommodation, with preservation of the light reflex. I might point out, however, that there is very often considerable difficulty in inducing the patient to accommodate for near vision, owing to the defect of attention, which is part of the disease; I have always found that when the patient can be persuaded to accommodate, the pupil contracts normally, except in cases where there is general sluggishness and limitation of all pupillary movements. The pupil condition in most of my cases was normal, confirming the usual description of the text-books. But I have occasionally met with a general sluggishness such as I have alluded to: in one case, the pupils were almost fixed for some weeks, yet recovered perfect movement as the neuritis improved; in this case, the associated mental confusion was profound.

The fact that mental disorder of some sort is almost invariably present in alcoholic polyneuritic cases is evidently of pathological significance, as showing that cortical

neurones are affected. One cannot too strongly insist that this mental disorder is an important part of the disease. Its prominent feature is, in most cases, a pronounced mental confusion, with disorder of observation, and failure of capacity for retaining recent impressions. Hence arises a defect of orientation as to time and place, and loss of memory for recent events, often with illusions as to the identity of persons. The "romancing," illustrated by the pseudo-reminiscences of imaginary journeys, depends probably upon this defect. The disorder was well exemplified in Cases 1 and 3.

The late Prof. Korsakow, of Moscow, showed that the same "polyneuritic psychosis" might occur in neuritis from any toxic cause, though there can be no doubt that alcohol is incomparably the most frequent. During the last three years, I have had under my observation at Colney Hatch fourteen cases of alcoholic neuritis, all with more or less characteristic disorder, without counting Case 2, in which there was a "delirium." And of fourteen other cases which I examined in Poor-Law Infirmaries, all presented marked confusion, and might equally well have been certified as insane. Certification, however, seems to be determined largely by collateral circumstances, such as the number of available beds, or the question whether the patient is in any way troublesome, or is physically fit to be removed to an asylum. The cases met with in the asylum do not differ in any essential respect from those seen outside. But, in both groups, though the defect of attention, memory and orientation is seldom wanting, other features are variable.

The mental disorder is doubtless related in some way to the cortical changes. The striking feature in each of my cases is that the Betz-cells and other large pyramids show the very same type of change as that seen in the anterior cornual cells. With this, there is diffuse, bilaterally symmetrical degeneration of many of their related fibres in the pyramidal tracts. Horizontal sections of the internal capsule show (in addition to degenerated pyramidal fibres) very numerous degenerated fibres in the anterior limb, which disappear in the gray matter of the thalamus; these

apparently connect the thalamus with the motor and frontal cortex, but I have not been able to decide whether they belong to cortical or to thalamic cells. The tangential fibres of the upper motor region were examined in Case 1, and showed a slight degenerative atrophy, as in Jolly's cases.

The combination of this so-called "axonal" cell change with fibre degeneration in the cortical neurones is identical with that seen in the peripheral neurones. Thus, alcoholic neuritis is not peripheral merely, for its characteristic lesion is equally marked in higher neurones which are entirely central. Meyer found a similar condition in eight cases of "delirious and depressive disorders," and speaks of it as "central neuritis." As in his cases, so in mine, the changes in the cortical vessels and neuroglia are very slight, and seem quite insufficient to account for the cell changes. As in his cases also, focal production of the fibre lesions can be excluded absolutely in Cases 1 and 3, and with extreme probability in Case 2. There is clearly a selective affection of neurones. In Cases 2 and 3, the more acute "central neuritis" appears to be superimposed upon an older peripheral neuritis. In Case 1 both are seen in the acute stage together.

Reports of the occurrence of this Betz-cell change (with or without mention of pyramidal tract degeneration) in cases of polyneuritis, appear to be limited to two cases by Faure,[1] one by Turner, and one by Wright and Orange; that it was present in Wright and Orange's case is shown by their diagram rather than by their not very lucid description. To these I would now add my three cases. It seems likely that this cortical change may be common, or usual, in alcoholic neuritis; it has apparently been seldom looked for, as descriptions of cortical cells in this disease are extremely few. The point of interest is that the lesion of cortical neurones is now brought into line with that of peripheral neurones.

The special form of Betz-cell change seen in these

[1] These appear to be the same two cases as those reported by Ballet and Faure.

examples is not confined, however, to cases of definite and pronounced peripheral neuritis, but is also found in other alcoholic, delirious and confusional disorders.

Cases which present, on the clinical side, some form of psychosis, and on the pathological side, an "axonal" Betz-cell change or "central neuritis," appear to group themselves under the following heads:—"Polyneuritic psychosis," with or without recognised peripheral neuritis (Faure, Wright and Orange, Turner), delirium tremens (Ewing, Bonhœffer), various sub-acute delirious conditions (Meyer), confusional states, often with depression (Meyer, Turner, Cauria), and perhaps Landry's paralysis, when associated with cerebral symptoms (Worcester). This list is necessarily imperfect as a classification, for there is considerable overlapping of types. We have to do with a group of closely allied disorders, including many intermediate mixed forms.

Though we are not in a position to state that these are all pathologically identical, we can at any rate say that, in addition to this similarity of microscopical appearances, they present many interesting points of resemblance in their etiology, pathology, symptoms and physical signs. The generalisation thus dimly foreshadowed may prove to be less fantastic than it at first sight appears.

To the demonstration of the similarity of these affections as regards cortical changes, afforded by the researches of those whose names I have given in brackets, I would endeavour here to add a rough outline of some of their miscellaneous clinical resemblances.

Such experience as I have is quite in accordance with Jolly's observation, that a very close relationship exists between the polyneuritic psychosis and delirium tremens. Frequently in cases of marked neuritis there is, in addition to the confusion, a delirious condition, indistinguishable from delirium tremens, with marked tremor and jactitation, and often characteristic visual hallucinations (as in Case 2). In ordinary delirium tremens we find the same marked defect of attention, memory and orientation: Kraepelin mentions the occurrence of pseudo-reminiscences, and delusions as to the identity of persons around: and very

often, as Jolly has observed, at the height of delirium tremens slight neuritic symptoms appear, such as tenderness of muscles to pressure. The neuritic psychosis is often at its onset exactly like delirium tremens, though afterwards it may pass into a condition corresponding more to Korsakow's type; and many neuritic patients whose symptoms in the daytime are mainly confusional, at night are restless and delirious, with auditory or visual hallucinations, the latter being frequently of the same type as those seen in delirium tremens (animals of various kinds, &c.); and there is often a distinct element of fright, or dread, sometimes with delusions of physical torture. It may be difficult to decide whether a given case (*e.g.*, Case 2) is a delirious neuritic psychosis, or a delirium tremens; the question indeed seems little more than a quibble.

In the polyneuritic disorder, as in delirium tremens, there is often marked defect of co-ordination and equilibration; and each of my three cases shows a degeneration in the white matter of the cerebellum, especially of the vermis, similar to that which Bonhœffer found in delirium tremens. As also in some of the cases of delirium tremens which Bonhœffer has described, so, in the neuritic cases, one not infrequently observes symptoms suggestive of focal lesion of particular cortical areas, yet without any macroscopic meningeal or vascular change. These symptoms, though severe at the time, often pass off so rapidly and completely, that the diagnosis of gross lesion is soon shown to be erroneous. Thus, in the second week of my Case 1, there was a condition of coma with hemiplegia, corresponding to which the pathological examination revealed nothing. Coma was complete for forty-eight hours; the hemiplegia gradually passed off in the course of the next eight days. In Case 2, one might perhaps at times have been inclined to suspect some lesion of the visual area; if one made a feint to strike the patient, there was not even a reflex closure of the lids, though her eyes were wide open, and she was talking at the time; the head and eyes were nearly always turned towards the left, especially when the visual hallucinations were active. As in delirium tremens, irregular

jactitation, and also rhythmical convulsive clonic jerking of the limbs, of a somewhat significantly epileptiform type, are frequently observed in polyneuritic cases, as in Cases 1 and 2, and, to a less extent, in 3. These irritation-phenomena are doubtless of cortical origin.

There is an overlapping of types, not only between delirium tremens and the neuritic psychosis, but also between each of these and the other disorders I have mentioned.

Alteration of the reflexes is common in all, but varies according as the cortical or the peripheral lesions predominate; if the former, then rigidity of the limbs may also be observed.

Meyer thus sums up the clinical features in his eight cases of "central neuritis": "After a course in which there is no suspicion of organic disorder, there appears, more or less suddenly, difficulty of locomotion, increasing weakness for co-ordinated movements, at times jactitations of the limbs, and rigidity, and disorders of the reflexes, often together with diarrhœa and occasional febrile fluctuations; the mental condition is either that of anxious perplexed agitation, delirium, or stupor, similar to a protracted delirium tremens." There was evident defect of orientation in his Cases 2, 3, 5, 7, 8, doubtful in Case 1, and none was made out in Cases 4 and 6. An alcoholic history was present in Cases 5 and 8, denied in Case 7, while as to the others there is no statement. There was a history of lead-poisoning in Cases 4 and 6, which is somewhat significant in view of the well-known tendency of lead to induce neuritis. Many features of Meyer's cases suggest some form of toxæmia.

It is interesting to compare my Case 2 with these examples. The patient, as the result of a fracture, developed within a few hours what appeared to be a delirium tremens, with the usual tremor, excitement, and tactile and visual hallucinations of cats, dogs, &c. But instead of terminating in the usual way in rapid recovery or death, the condition was protracted for ten weeks, and there were observed the same rigidity of the arms, obstinate refusal of food, and slight diarrhœa before death, as were presented by

Meyer's cases; while, in addition, there was polyneuritis, and the spontaneous clonic movements of the limbs so frequently seen in polyneuritic conditions.

In all these various disorders—delirium tremens, neuritic psychosis, confusional insanity, &c.—in addition to the defect of memory and orientation, the pseudo-reminiscences, visual hallucinations, excitement, tremor, speech disorder, jactitation, rigidity, alteration of the reflexes, and so forth, there may be also hallucinations of threatening voices, delusions that food is poisoned, obstinate refusal of food (as in my Cases 2 and 3), and delusions of physical persecution and torture. In all these conditions there is frequently also marked depression, almost deserving the name of melancholia.

It may be observed in passing that in Korsakow's type of neuritic psychosis, the melancholic factor is sometimes incidentally illustrated in a curious way by the romancing. I have several times noticed that the imaginary journeys have been either fruitless, or attended by some mishap, such as a fall (*cf.* Case 3) or sudden illness, or a fright from a runaway horse; or the patient tells us that she found her mother very ill; or she sends her little girl to fetch the supper beer, but the child drops the jug as she is bringing it home. The pseudo-reminiscence of these imaginary misfortunes is the occasion for tears.

With regard to confusional insanity, it may be pointed out that Korsakow's "polyneuritic psychosis" is really a marked form of confusional disorder. Meyer's "delirious and depressive" cases are closely allied, not only to delirium tremens, but also to the neuritic psychosis and confusional insanity. He does not appear to have examined any of the nerves in his cases. In my experience, slight neuritis is not very uncommon in alcoholic confusional states, but it requires to be systematically looked for. In Cases 2 and 3, it was by no means obvious clinically, though there was extreme atrophy of the tibial nerves.

As to Landry's paralysis, I would simply remark that in Worcester's case there were somewhat analogous mental symptoms, and also that Ross and Bury have shown that,

as regards the peripheral affection, no hard and fast line can be drawn between Landry's paralysis and polyneuritis.

Jolly's observations show that in some cases of neuritis the mental disorder may be very slight (possibly, even, altogether absent), and that, on the other hand, Korsakow's polyneuritic psychosis may occasionally occur without definite peripheral neuritis. Side by side with this may be set the pathological observation of the occurrence of this neuritic lesion of cortical neurones in certain cases apart from recognised peripheral neuritis; to Meyer's cases, and those he quotes, may now be added those of Cauria. There is no doubt that in certain patients the cortical neurones are the more vulnerable, and in others the peripheral. Our conception of neuritis must be widened, and not restricted to so-called typical cases. The selective action of the toxic agent (whatever it be) is clearly modified by differences of resistance of the various neurone systems, depending largely on hereditary and developmental factors, and the occupation and habits of the patient. Even in mere drunkenness, one man's liquor flies to his head, and another's to his legs.

We have seen that the neuritic, delirious and confusional conditions displaying this characteristic cortical change present numerous clinical resemblances. They also have much in common as regards their etiology.

Neither polyneuritis, delirium tremens, nor the confusional disorders can be regarded as the expression of a mere alcohol-poisoning. They have a more complex etiology, and present the characters of a severe general disease, of the nature of a toxæmia, depending probably on an auto-intoxication from disordered metabolism. They may, most of them, result from other poisons besides alcohol, though their appearance is evidently favoured in a very special way by chronic alcoholism. But they only result indirectly from the alcoholism, and require the co-operation of various contributory or exciting causes, such as shock, surgical injury, chill, pneumonia, tuberculosis and other febrile and afebrile illnesses, want of food, the onset of the menopause, &c.; Judson Bury mentions cases of polyneuritis following injury

to the head. The patient may have been addicted for years to alcohol, but the introduction of one of these additional factors suddenly gives rise for the first time to one or other of these disorders.

Moreover, all of them, but especially neuritis and delirium tremens, present a series of features directly suggestive of an auto-toxic origin. Not only do we see that many of their contributory causes are of a kind eminently calculated to cause derangement of metabolism, but we cannot fail to note the frequent occurrence of circulatory disturbance, rapid pulse, acute fatty degeneration of the heart and skeletal muscles, pyrexia without recognisable cause, profuse paroxysmal sweats even in afebrile cases, albuminuria, and sometimes diarrhœa as the end approaches; while, at least in delirium tremens, there is an alteration of the blood-count, with increase of polynuclear leucocytes, and diminution of eosinophile cells (Elsholz). All these phenomena are strongly suggestive of a severe toxæmia; and so also, I think, are many of the nervous manifestations—such as the various sensory disturbances, the motor weakness, tremor, inco-ordination, giddiness, speech disorder, twitchings of muscles, and epileptiform convulsions. Jolly has pointed out the toxic significance of many of these, both in delirium tremens and in neuritis. They remind us of the analogous symptoms seen in acute alcohol-intoxication. Similar suggestive features are far from uncommon in many other delirious and confusional states.

The frequent chronic gastritis, and the fatty, cirrhotic, and other disorders of the liver and kidneys, may be etiologically important. Cirrhosis of the liver, however, was very slight in two of my cases, and absent in the third, supporting the generally accepted opinion that marked cirrhosis is uncommon in neuritis, and perhaps also suggesting that the toxæmia does not set up neuritis unless at the same time there is nervous instability. Beer was a factor in Case 3, but not in the other two; the cases I have seen do not support the theory that arsenic is always a factor in alcoholic neuritis, but rather suggest that spirits are an important cause. This is consistent with the auto-intoxica-

tion theory, inasmuch as it seems to add weight to the gastro-intestinal and hepatic affections. The choline present in the blood in great quantity in Case 1 is, of course, of no etiological significance; it simply indicates the great amount of myelin degeneration in progress at the time of death.

The fact that the so-called "axonal" Betz-cell change is seen in acute forms, like delirium tremens, is opposed to the view that it is secondary to an axis-cylinder affection. And in my Case 3, as in some of the cases of Meyer and Faure, though the pyramidal tract degeneration was comparatively slight, *all* the Betz-cells showed this change. In the acute cases the cell changes far outweigh the fibre degeneration; the latter appears to be simply a secondary manifestation of the disorder of the neurone. The cell changes are almost certainly primary. In some of Bonhœffer's cases the changes in many cells showed characters approaching those of Nissl's "acute alteration," which is good evidence of a primary affection. In other delirious cases clinically indistinguishable, he found a much more definite "axonal" type; his description[1] would apply accurately to the cells in my neuritic cases, and so also would Ewing's.

In all these varieties of nervous disease occuring in alcoholic patients, the affected neurones, central and peripheral, present the same essential lesion—a cell change of distinct type, with or without degeneration of the myelin sheath of the parts most remote from the cell. The changes in the neurone do not begin in the prolongations, but express a disorder which leads to such general impairment of the whole neurone, that the parts furthest from the trophic centre degenerate. The affection is polyneuronal rather than polyneuritic. In all forms, we have to do with a general toxæmia, affecting whole neurones of many different orders throughout the nervous system, and rarely or never affecting peripheral neurones only. In some cases the peripheral neurones are the more vulnerable, in others

[1] "Die grossen Pyramiden; der Zell-leib nicht gleichmässig tingiert; einzelne fast ganz farblose Stellen; die farbbäre Substanz zeigt in einzelnen Zellen noch Reste der parallelen Anordung; namentlich in der Peripherie sind zahlreiche grabkörnige Partikelchen; die Fortsätze sind nicht abnorm lang; der Kern ist wandständig, gross, blass."

the central. Hence in some cases the "peripheral neuritis" predominates, in others the "central neuritis." Thus the physical illness is closely related to a number of affections which come within the province of the alienist. The typical case of severe peripheral neuritis, familiar in the hospital ward, is connected by any number of intermediate mixed forms, with several varieties of confusional insanity, delirium, and allied disorders, in which there may be no appreciable peripheral affection.

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CASE SHOWING (1) DEFECTIVE DEVELOPMENT OF DURA MATER, (2) OLD MENINGITIS, AND (3) INTERNAL HYDROCEPHALUS.

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At an autopsy on the body of an idiot male, aged 40 years, the following facts were noted.

The skull-cap was thin and dense, and somewhat asymmetrical, being flattened anteriorly and to the left. Dolicocephaly was present to a considerable extent. The external surface of the dura mater appeared normal. There was no thickening nor undue adhesion. The falx cerebri was absent, except for two minute folds—one an inch in front of the olfactory bulb, the other at the level of the occipital lobes. The tentorium cerebelli was absent except a small portion on each side which projected inwards for about an inch at its widest part. A small ridge represented the falx cerebelli. The pia-arachnoid was thickened and opaque, especially over the vertex. The great longitudinal fissure was obliterated by pia-mater, the arachnoid passing uninterruptedly over it. The interval between cerebrum and cerebellum was similarly obliterated, pia-mater uniting the one to the other, except where the portions of the tentorium were present. The thickening and adhesion of the pia-arachnoid was much less marked on the base of the brain. The meningitis had been mainly lateral and vertical, especially the latter. There was considerable thickening and adhesion about the Sylvian fissures. There was a moderate amount of clear fluid in the subarachnoid space, much in the cisternæ magna and pontis. The brain mantle was wasted. The cerebrum was nearly symmetrical, the convolutions of natural arrangement.

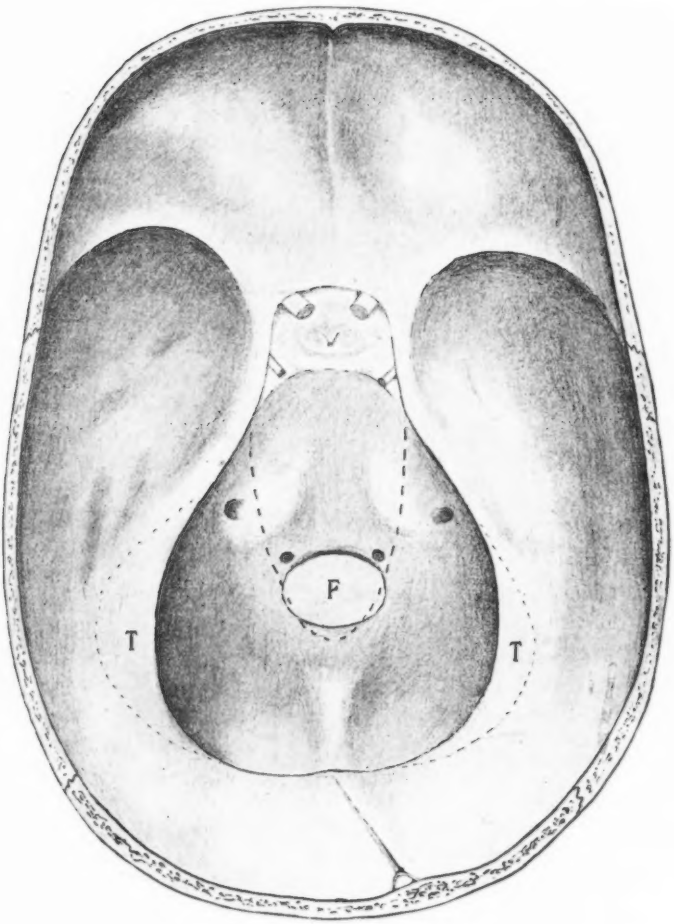

FIG. I

On making a frontal section of the brain, the interior was found to consist of one large cavity, the various ventricles having united into one. The cavity was five inches long, and three and a half inches broad. The cornua of the lateral ventricles were much dilated. The structures in the region of the fifth ventricle had entirely disappeared. The roof of the cavity was formed by white matter laterally, and centrally by a somewhat flattened corpus callosum, on the under surface of which were irregular rounded tubercles of gray matter. The floor of the cavity owing to the fusion of the third with the lateral ventricles became practically the normal floor of the third and lateral ventricles, though much more of optic thalamus and caudate nucleus was visible than usual. The posterior cornua had fused with the suprapineal recess which was much distended. The aqueduct of Sylvius was of the usual calibre.

The patient is stated to have had scarlet fever when 3 years old, and to have been imbecile ever since.

One must assume that the abnormalty of the dura was congenital. Probably the meningitis would be a complication of the scarlatina, and, owing to the absence of dura mater, one can readily understand the adhesion of cerebrum to cerebellum, and of the two lobes of the cerebrum to one another along the great longitudinal fissure. The meningitis would, of course, also cause the internal hydrocephalus by blocking the means of communication from the ventricular cavities to the subarachnoid space.

DESCRIPTION OF FIGURES.

FIG. 1.—*A view of the base of the skull showing the defective development of the tentorium cerebelli* (*T*).

The normal outline of the tentorium is indicated by the coarsely dotted line, while the finely dotted line indicates the situation of the lateral sinus. Posteriorily is seen the remains of the falx cerebelli as a very thin ridge displaced to one side. *F.* Foramen magnum.

FIG. 2.—*Photograph of Frontal Section of Brain through tips of Cunei.*

The pia-arachnoid fills up the great longitudinal fissure, and the greater part of the interval between the cerebrum and cerebellum, there being no falx cerebri, and the tentorium being absent except as indicated laterally.

The lateral ventricles are very considerably dilated, and have been fused into one cavity. The posterior cornua have fused with the suprapineal recess, which is also much distended.

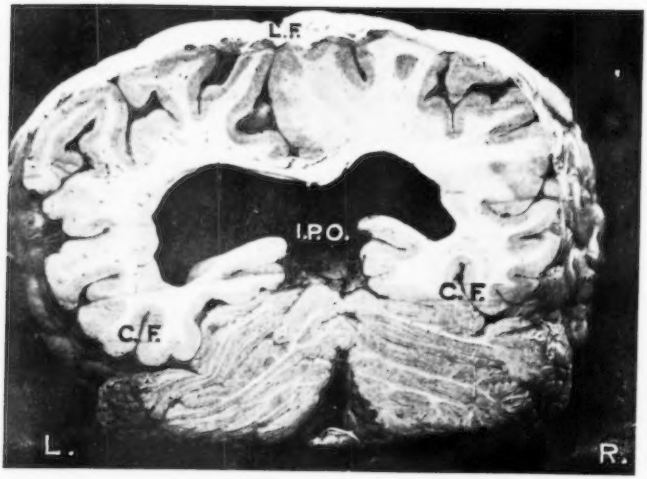

FIG. 2.

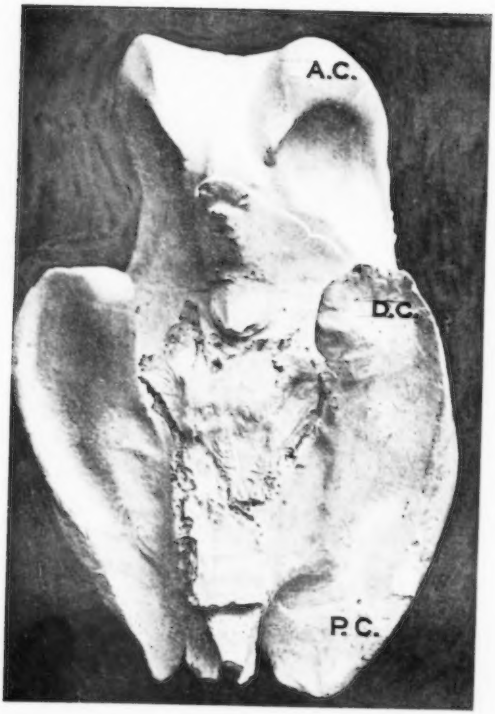

FIG. 3.

The arachnoid passes uninterruptedly over the great longitudinal fissure, which is displaced to the left and passes in a curved direction inwards.

The cerebellum is united to the cerebrum by pia-mater, except for about an inch on each side, where there is a depression into which the portion of the tentorium which is present dips.

The brain mantle of the cerebrum is much wasted.

The cerebellum is not wasted nor otherwise changed in naked-eye aspect.

FIG. 3.—*Photograph of Cast of the Fused Ventricular Cavity (under surface).*

The irregular surface in the centre is due to the vessels of the choroid plexus.

A.C. Anterior cornu.
D.C. Descending cornu.
P.C Posterior cornu.

For this cast I am indebted to Dr. J. O. Wakelin Barratt, late pathologist to the West Riding Asylum, Wakefield.

PAIN.[1]

BY JAMES MACKENZIE, M.D.

Burnley.

I.—Introduction.
II.—Definition.
III.—The pain of the digestive tract.
IV.—The pains due to gastric ulcer.
V.—Superficial and deep cutaneous hyperæsthesia.
VI.—The absence of spinal nerves from serous membranes.
VII.—Muscular hyperæsthesia.
VIII.—The viscero-muscular reflex.
IX.—The results of stimulation of exposed viscera.
X.—Testicular pain.
XI.—The mechanism by which the sensory symptoms in visceral disease arise.
XII.—Some theoretical considerations.

I.—Introduction.

I FEEL some hesitation in appearing before you with such an array of facts as I intend to present. The observations I have made have involved no deep or prolonged investigation, but are mainly the clinical symptoms that are found in the routine examination of patients. The deductions I have drawn from these symptoms are opposed to all the teaching and traditions of the profession. Though I am myself convinced of the justness of my deductions, I fear that my presentment of the reasons of the faith that is within me may not carry conviction to your minds. I trust, however, that it will cause some of you to enquire whether these things be so or not.

In the first place, might I ask you to approach this subject untrammelled by any preconceived ideas, and even to dismiss from your minds, if it be possible, the results of your own experience. My reason for this suggestion is that

[1] Read before the Neurological Society of London, October 23, 1902.

hitherto the consideration of the sensory symptoms have been based on an imperfect appreciation of the situation in which the symptoms were felt. Thus, for instance, a leading authority describes a tenderness of the heart muscle as a symptom of myocarditis, because he found that when he pressed his finger over the heart pain was felt. Or again, a tender liver is frequently recognised, because pain is felt when pressure is applied over the organ. In such cases the observation is unreliable, because no means are taken to ascertain the sensitiveness of the tissues between the finger and the organ. Similarly peritonitis is commonly supposed to be present when there is hardness of the abdominal wall with pain on pressure; for it is usually assumed that the pain arises from stimulation of the sensitive peritoneum, without considering that sensitive structures external to the peritoneum are being stimulated.

But not only have clinical observers drawn too hasty conclusions, but physiologists are not a little to blame for fostering an erroneous view in regard to the functions of certain of the sympathetic nerves. One frequently meets in physiogical writings the bald statement that certain nerves in the sympathetic or certain ganglia in the viscera are sensory in function. Those who, like myself, have implicit faith in the law and the prophets, as represented in physiological text-books, never dream of disputing physiological dogmas. But when I reached a certain stage in the study of this subject, I was led to enquire upon what this dogmatic assertion was based. I must confess I have not been able to find a single fact in support of it, apart from the fact that certain sympathetic nerves are afferent in relation to the spinal cord. Nay, further, in considering this matter I do not see how any evidence can ever be available as a result of experimental observation on animals. If a stimulus adequate to produce pain be employed and the animal shows symptoms of pain, no evidence is forthcoming to show in what region the pain is felt. Many experiments have demonstrated that the viscera in the conscious animal may be grossly injured without the animal evincing the slightest evidence of sensation. In this latter case all that has been proved has

been that the stimulus has not been adequate, for we all know from personal experience that the viscera can manifest the symptom of pain.

II.—Definition.

The purpose of this paper is to place before you some of the reasons that justify me in suggesting the following definition of pain:—

Pain is a disagreeable sensation due to the stimulation of some portion of the cerebro-spinal nervous system, and referred to the peripheral distribution in the external body wall of cerebro-spinal sensory nerves.

In this definition a distinction is made between the sympathetic nervous system and the cerebro-spinal. The clinical facts demonstrate that though stimulation of one system may react on the other, their functions are totally distinct, and, therefore, so far as the subject in hand is concerned, the symptom of pain is purely a cerebro-spinal function.

The above definition implies that the sensation of pain from whatever source the stimulation arises, is referred to the peripheral distribution of sensory nerves in the external body-wall, whether it arises in the brain (as in the rare cases where pain in a distant part of the body is an aura of epilepsy); in the spinal cord (as in locomotor ataxia); in the posterior root ganglia (as in herpes zoster); in the external body-wall, or in the viscera (as it will be the purpose of this paper to demonstrate).

The data on which the foregoing propositions are based are derived entirely from clinical observations. From what I have said, I consider that experimental observations on animals are of no use in deciding this question. It is only from the conscious human subject that reliable evidence can be obtained.

In studying this subject, there are two difficulties against which one has to be on guard. The first of these is the imperfect recollections of the site in which the patient has felt the pain. This can be avoided usually by getting the patient to note accurately where the pain was felt during

a subsequent attack, or by watching the patient when actually suffering from pain. The second difficulty is a tendency for the observer to find only that of which he is in search, neglecting any symptom that does not accord with his preconceived ideas. I must confess I have found it necessary to put a control on my own observations by having them verified by a colleague. In making my observations I invariably had the most striking and important cases examined independently. Such phenomena as my colleagues could not verify I rejected, for if these sensory symptoms are to be of value they must be capable of being elicited by observers free from bias. Cases should not be recorded that are based upon recollections alone, for it is wonderful how far from the truth the memory may wander when there is a favourite theory to be advanced.

In bringing forward the arguments in favor of the foregoing definition I will deal with the subject partly in an autobiographical form, setting forth the reasons that gradually forced me to the evolution of the definition. I may say that it is more than fifteen years since the idea of this definition arose in my mind, as an explanation of certain observed facts. At first it was formulated with certain reservations and exceptions, but as time went on the difficulties and objections gradually disappeared as I employed more thorough and exact methods of observation. It was only within the last two years that the final objections were removed, and it is but recently that I have felt sufficient confidence in the truth of the definition as to justify me in publicly upholding it.

III.—The Pain of the Digestive Tract.

For many years it had been my custom when writing down patients' symptoms to note the seat of pain, when it was abdominal by quickly drawing the lines which divide the abdomen into areas and marking the situation of the pain by a cross or by a wavy line. On glancing over these notes I was struck with the constancy with which pain was referred to certain areas. Thus in gastric affections the great majority referred the pain to the epigastrium. As

amongst these patients there were a large number of cases of gastric ulcer, it seemed to me strange that if the pain were situated in the ulcer so many should have ulcers in the epigastric region. I also made this further observation, that in gastric ulcer when the pain was severe and limited, so that the patient would unerringly place her finger over its site, that the situation of the pain was constant when the patient took a deep breath and manifestly altered the situation of the stomach. Similarly the pain remained constant during peristalsis of the stomach and whether the stomach was full or empty. About this time I had two cases of gastric ulcer where the sites of the ulcers revealed at the *post-mortem* examination bore no relation whatever to the seat of pain during life—an observation which later experience has fully corroborated.

In continuing my observations on the digestive tract I found that the severe pains that accompany obstruction of the bowel never descended lower than the umbilical area when the obstruction was situated in the small intestine. Numerous causes have been assigned for the production of pain in obstructed bowel but there can now be no doubt, as I shall subsequently show, that it is due to the powerful peristalsis of the bowel. Peristalsis never occurs below the point of obstruction. It is my experience to meet with and to operate on a goodly number of cases of strangulated hernia. I usually make careful note of the site of pain in these cases. I have never yet found the severe colicky pains that are present descend lower than the umbilical area, when the obstruction was in some portion of the small intestine. In a few cases of obstruction of the bowel from other causes, I have been able to locate approximately its situation in the small intestine by noticing how far down in the umbilical area the pain was felt.

In a few cases of obstruction in the great bowel where the obstruction occurred at the splenic and sigmoid flexures I had noted that the pains descended lower than the umbilical area. But these cases are too few for me to dogmatise upon. We have, however, other means for testing where the pains due to peristalsis of the great intestine are felt. If

a large enema be given and the individual requested to forcibly retain it, powerful peristalsis is set up in the great intestine. The pain resulting is invariably referred to a limited area immediately above the pubis, usually extending across the middle line.

As a result of these observations I have formulated the view that in pain due to the digestive tract, the pain is felt across the middle line of the abdomen, and in regularly descending areas according as the region affected passes from the stomach to the great intestine—the epigastric area being the region for stomach pains, the umbilical area being the region for pains of the small intestine, and the hypogastric area being the region for pains due to the great intestine. Many observations have justified the correctness of this view. One striking instance which is common to most people at various times is the fact that when colicky pains arise which convince the sufferer he is about to have an attack of diarrhœa, so long as the pains are felt in the neighbourhood of the umbilicus relief will not be at once forthcoming. But as time passes the pains gradually descend lower and lower and when they reach near to the pubis the call for relief becomes urgent and imperative.

IV.—The Pains due to Gastric Ulcer.

Arising out of this view, that the pain in the abdominal wall bears a relation to the portion of the bowel stimulated, my observations in regard to the site of pain in gastric ulcer are of importance. As I have said, I found the situation of the limited area of pain in gastric ulcer to be in the epigastric region, sometimes high up in this area, sometimes situated low down. I then formulated the view that probably the higher the pain the nearer would the ulcer be to the cardiac end of the stomach. This view has been verified in seven instances where I have had *post-mortem* examinations and in six cases where the site of the ulcer was discovered by operation. To illustrate, not only the justification of this view, but more important, its practical utility, I will cite three typical instances. A girl, aged 14 years, who had had

pain after food for many months, referred the situation of the pain with great precision to a spot in the middle of the epigastric region. She was suddenly seized with collapse and severe pain over the upper part of the abdomen. There could be no doubt that it was a case of perforation of the stomach. Within eight hours we opened the abdomen, and as I had noted the situation of the pain previous to the rupture, I suggested that the ulcer would probably be found in the middle of the stomach. The incision was therefore made well to the left of the middle line. The perforation was readily met with in the middle of the stomach on the lesser curvature, stitched up, and the patient made an excellent recovery.

In another case where I was called into consultation twenty hours after the perforation had taken place, the patient had suffered for many months from pain after food. She located the site of this pain with great certainty in the upper part of the epigastrium, over the xiphisternum. I reasoned from this that the perforated ulcer would be near the cardiac end of the stomach. The incision opening the abdominal cavity was, therefore, made as far to the left as possible. On opening the abdomen there was found a large quantity of fluid, and a considerable quantity of flaky lymph covered most of the exposed organs. The stomach was carefully searched, and we found it rather firmly adherent at the cardiac end to the posterior wall of the abdomen. We inspected the whole of the stomach except the adherent part, and there can be no doubt that the adhesions surrounded the ulcer. We resolved not to break down these adhesions, as it would have been impossible to drag this portion of the organ sufficiently far out to enable us to stitch it. The abdomen was very efficiently flushed, the wound stitched up, and the patient made a good recovery.

Another case had been under my care for ten years, for repeated attacks of epigastric pain. She consulted an eminent surgeon who wrote me stating that the patient had an ulcer in the middle of the stomach and on the posterior wall, and he recommended an operation for her

relief. I re-examined the patient and made the following note: that, inasmuch as the pain is situated at the lowest part of the epigastric region, and as there is also here a limited area of tenderness of the skin, the ulcer should be found at the pyloric orifice. This latter view was verified at the operation subsequently performed.

V.—Superficial and Deep Cutaneous Hyperæsthesia.

Another observation I made confirmed me in the impression that the pain of visceral disease was felt in the peripheral distribution of a cerebro-spinal nerve was the detection of cutaneous hyperæsthesia in the areas where the pain was felt. This observation was made in 1891. A patient who had had an attack of gall stone colic, called on me, holding his arm stiffly away from his side. Asked why he carried himself in this manner, he replied that the friction of his clothes against his side caused him great pain. I had him stripped, and found an area of cutaneous hyperæsthesia extending irregularly over a large portion of the upper part of the abdomen and lower part of the chest, limited entirely to the right side. After this I examined systematically a large number of patients, and I found that frequently after an attack of pain, the skin remained hyperæsthetic for a varying period. When present, the hyperæsthesia invariably appeared in the region where the pain had been felt, and followed the distribution of the pain. Thus in angina pectoris I have found the hyperæsthesia limited to a small portion of the skin on the outer part of the left chest wall, exactly in the region where the pain was felt. With recurring attacks the pain became more severe, extending over the whole precordium, then into the armpit, and down the inner side of the arm. The hyperæsthesia extended in exactly the same way.

As a result of a very large number of observations, the following are the conclusions I have come to in regard to the occurrence of hyperæsthesia in visceral disease. It occurs in the peripheral distribution of those spinal nerves

whose centres in the spinal cord are connected with the sympathetic nerves supplying the affected organ. It generally embraces portions of the distribution of more than one nerve. As it extends it does not affect the complete distribution of one nerve before appearing in the areas supplied by a contiguous nerve. Thus, in hyperæsthesia associated with heart affections, the hyperæsthesia may be present only in the skin covering the precordium, that is, in an area supplied by portions of the fourth and fifth dorsal nerves. As the hyperæsthesia extends it does not complete the distribution of these two nerves by extending round to the back. Rather it passes to the axilla and arm appearing in portions of the areas supplied by the third and second dorsal nerves.

The cutaneous hyperæsthesia occurs in two forms, a superficial and a deep. The former can be shown by lightly stroking the surface of the skin by a pin head. The deep form is elicited by lightly grasping the skin and gently pressing it between the finger and the thumb, or it can be shown by direct pressure. The deep kind of hyperæsthesia may be present when the superficial is absent, but is always present along with the superficial. I desire to emphasise the importance of this distinction, because, in the absence of the superficial form of hyperæsthesia, pressure over an organ may be assumed to cause pain in the organ, when as a matter of fact it is the sensitive skin that is eliciting the pain. Before I recognised this difference, I was much hindered in the study of this subject.

The borders of the hyperæsthesia are always ill-defined. The patient cannot accurately state where the skin becomes hyperæsthetic, and portions of skin evidently hyperæsthetic at one time, when tested a few minutes later are found not to be hyperæsthetic. This peculiarity also occurs in the hyperæsthesia due to herpes zoster and to organic lesions of the cord. Whether it occurs in all cases of organic lesions of the cord I cannot say, as my observations have been in only a few cases. This indefinite border is of importance, as it verifies Sherrington's observations of the over-lap in the distribution of spinal nerves.

VI.—Absence of Spinal Nerves in Serous Membranes.

Although I was able to demonstrate that pain due to visceral disease was in many cases situated in the skin, yet there were a large number of cases that showed pain when pressure was applied over an abdominal organ when there was no sign of cutaneous hyperæsthesia. The recognition of the deep form of cutaneous hyperæsthesia accounted for a considerable number of such cases. But there was left a large residue, where there was tenderness on pressure and no cutaneous hyperæsthesia. It appeared to me that this might be due to a sensitiveness of the peritoneum, and the question arose in my mind: Was the peritoneum supplied by spinal nerves? I could get no help from anatomical works, and so I dissected a number of spinal nerves following them from their exit from the spinal cord to their final endings in muscle or skin. In not a single instance could I detect a twig entering either the pleura or peritoneum.

VII.—Muscular Hyperæsthesia.

For a long time I was puzzled to explain the apparent clinical fact that the abdominal organs were tender to pressure. But examining the cases more minutely I found out at last the true explanation. The organ that presents itself most readily for demonstration is the liver. Enlargement of this organ especially when it occurs rapidly, as in certain cases of heart failure, is very often accompanied with a good deal of pain, readily elicited by exerting pressure over the organ. In such cases if the edge of the liver be carefully marked out, and light pressure applied with the finger so as to produce pain, it will be found that the tender area extends much lower down than the liver edge. If, after ascertaining that there is present neither form of cutaneous hyperæsthesia, one deftly raises a portion of the muscle of the abdominal wall, on the right side, and lightly presses the muscle it will be found that it is the muscle itself that is exquisitely sensitive. Since making this observation I have been able to demonstrate that the pain which is caused by pressure over

the abdomen in visceral disease and in peritonitis is entirely due to muscular hyperæsthesia when there is no cutaneous hyperæsthesia present. When a muscle is hyperæsthetic contraction of the muscle is often accompanied by pain, sometimes of great severity. This is best seen in the violent pain that accompanies the contraction of the hyperæsthetic intercostal muscles in pleurisy. I am convinced that the pain of pleurisy is due to this cause and not to the rubbing together of the surface of the inflamed pleura as is supposed by some people. My reasons for this assertion are, first that the pleura is an insensitive structure, as I shall show later, and, second, that exactly the same form of pain may arise when there is no pleurisy present. Thus after a severe attack of gall stone colic I have found the abdominal muscles extremely tender to pressure. But not only the abdominal muscles, but many of the thoracic muscles on the right side. If one lightly pressed the pectoralis major at the axillary fold the patient complained of the pain. In like manner pressure over the intercosal muscles elicited pain. The movements of respiration were extremely limited, the movements of inspiration being checked by violent spasms of the intercostal muscles. The picture of the patient was exactly that of one suffering from an attack of pleurisy. I need also only refer to the remarkable resemblance of the symptoms of pleurodynia to those of pleurisy.

VIII.—The Viscero-Muscular Reflex.

Of even greater significance than the muscular hyperæsthesia is the contraction of voluntary muscles due to visceral disease, which I have ventured to call the viscero-muscular reflex. Although every clinical observer is familiar with the board-like hardness that the abdominal muscles assume in certain diseases, I doubt if in the whole field of clinical examination the value of any other symptom has been more incorrectly estimated. The muscles forming the abdominal wall have the power of contracting in limited sections and of remaining contracted for indefinite periods.

The limited hardness thus arising gives to the palpating hand the impression of a hard tumour or swelling of some abdominal organ. When this hardness of the muscle is accompanied by great tenderness, it is invariably assumed to be an evidence of peritonitis. One is struck in reading descriptions of cases by the remarkable variety of conditions for which this condition is mistaken, such as enlarged and tender ovaries, tumours, inflammatory exudations, localised and general peritonitis, contracted bowel. Surgeons have been known to express surprise at the mysterious disappearance of a tumour for the removal of which they have opened the abdomen.

The conditions giving rise to the contracted muscle are various. Peritonitis causes it, and as the muscle is also usually tender, these symptoms of hardness and tenderness of the abdominal wall have come to be looked upon as undoubted evidence of peritonitis. But these symptoms may be, and often are, present with absolutely no peritonitis. Thus I have found a tenderness with firm contraction of the lower part of the left rectus abdomnis muscle in a case of stone in the bladder with no peritonitis. Hardness and tenderness of the recti over the epigastrium is common in gastric ulcer, and I have found these symptoms without any peritonitis. I have also found hardness over a limited area in the left lumbar region due to a tubercular ulcer in the posterior wall of the descending colon, and there was no peritonitis underlying the hard and tender muscle. In like manner wide-spread tenderness of the abdominal wall with hard contraction of the whole abdominal muscles may occur without any peritonitis. As illustrating the prevalent notions of the meaning of this symptom I will cite the following case. I was summoned to a neighbouring town to operate upon a fellow practitioner for obstruction of the bowels. The symptoms were, no movements of the bowel for two days, nor had any flatus been passed; some vomiting, but not fæcal; considerable abdominal distension with great hardness of the whole abdominal wall, and pain on the slightest pressure. Some difficulty was experienced in passing the finger into the

bowel on account of the strong contraction of the sphincters. The patient had every few moments severe attacks of pain. The pain began in the left lumbar region passing forwards and downwards towards the pubis. The left testicle was very tender to pressure. From the situation of the pain and the tenderness of the left testicle I had no hesitation in recognising the condition as one of renal calculus. In my experience the pain in obstruction of the bowel is never so distinctly one sided. The inability to have the bowels moved was simply due to the violent contraction of the sphincters, such contraction, with the contraction of the abdominal muscles, being due to the renal calculus. The diagnosis was confirmed by the passage of a calculus next day with immediate disappearance of all the symptoms. This patient has had two subsequent attacks with a repetition of all the foregoing symptoms. The contraction of the muscles was undoubtedly due to a violent stimulus passing from the organ affected to the spinal cord. There the irritation spreads affecting not only the centres of the sensory nerves, but also the centres of the muscular nerves. These stimulated give rise to violent muscular contractions—the viscero-muscular reflex.

There are a few peculiarities of this muscular contraction. It is often long-continued, persisting for months, never relaxing. This one can understand; for, so long as the organ is diseased, so long may the stimulus be adequate to keep up the contraction. It also differs from the contraction of muscles due to stimulation from other causes. The contraction of a muscle in a limb due to—say a fracture of a bone or a dislocated joint—yields readily on the administration of chloroform. The muscular contraction arising from visceral stimulation does not, as a rule, yield readily to chloroform. Sometimes, indeed, the contracted recti add considerably to the difficulties of abdominal operations during the whole time the patient is under chloroform. Again, I have seen it persist for a considerable time when the patient is under chloroform and yield during an attack of chloroform sickness. I shall suggest a possible reason for this behaviour under chloroform later.

IX.—The Results of Stimulating Exposed Viscera.

For a number of years I have seized every opportunity to test the sensibility of the viscera and their serous coverings in the conscious subject when the organs were exposed by operation. I have stimulated the pleura and pericardium, and, indirectly, the lung and the heart, through openings made by the removal of pieces of ribs for empyæma. In no instance have I been able to elicit any sensation of pain. The same result has followed the stimulation of the peritoneum and bowel in such cases as colotomies. In one case I had an unique opportunity for noting the response of some abdominal viscera to stimulation. I was called in consultation to see an elderly man who had an umbilical fistula. He had for years suffered from an umbilical hernia, and had endeavoured to keep it back by tightly bandaging a pad over it. The skin had ulcerated over a wide area in the neighbourhood, and the bowel had ulcerated through. When he took a drink of water, a few minutes later the water would be squirted with considerable force through the umbilical opening. We decided to resect the bowel. The patient objected to chloroform, and as the skin was gone from the site of the incision, and as the exposed muscle was not very tender, we resolved to proceed without an anæsthetic. After the incision into the abdominal cavity was made the rest of the operation was performed with an entire absence of pain with one exception. That is to say, we broke down old and recent peritoneal adhesions, we resected a piece of bowel and underlying mesentery, and we stitched the bowel and mesentery without the patient experiencing any sensation. I also pinched the bowel, the liver, and the peritoneum at different parts, and no sensation was elicited. But there were occasions when the patient groaned with pain. When we had prepared the upper end of the bowel, we laid it to one side on a warm aseptic cloth. At certain intervals a wave of peristalsis would pass down this portion of the bowel, and from being a wide and flaccid tube the bowel became a thick fleshy rod. Whenever this occurred the patient groaned. When asked what was the matter he said

he felt severe pain. When asked where the pain was felt he passed his hand over the region of the umbilicus. Now the offending piece of bowel was lying at least 12 inches away from the area in which he felt the pain.

There are certain conclusions to be drawn from such a case as this. We know that the organs and tissues I found insensitive can give rise to the sensation of pain, for peritonitis is a painful complaint and so also are affections of the bowel and liver. All then that could be said was that my means of stimulation were not adequate to produce pain. But the stimulation applied was practically identical with that which we seek to find out the sensitiveness of an organ in clinical examination; namely, by applying pressure over an organ. If pressure applied to an exposed organ is not an adequate stimulus to produce pain it is a fair deduction that the pain which results from pressure over the organ covered by the external body wall is really felt in the external body wall.

When an adequate stimulus did occur in the above case, as when the bowel passed into peristalsis, the pain was not felt in the bowel but was referred to a situation some distance from the contracting bowel.

X.—Testicular Pain.

While I had thus gradually been getting a clearer insight into the meaning of the sensory symptoms associated with visceral disease, there was one readily demonstrated experiment which for years prevented me asserting the truth of this definition of pain. I refer to the result of applying pressure to the testicle. In ordinary cases where the cord is short the pains felt on applying pressure to the testicle are not readily discriminated. If, however, an individual with a long cord, where the testicle hangs down a long way from the groin be examined, the pains resulting from pressure on the testicle are readily differentiated. In such a case a pain is felt at once and readily localised over the point of pressure. A few seconds later another pain is felt gradually increasing in intensity, and gradually passing away and referred to the groin.

That the first of these pains was not due to the stimulation of the tissues of the scrotum, could be shown by pressing on them apart from the testicle. It was this fact that here there were two distinct pains one, the pain in the groin, referred, the other undoubtedly situated in the organ, that for years prevented me being wholly convinced of the truth of my definition. But like all the other objections it yielded in course of time, and from being a stumbling block to the acceptance of the definition, has become the strong argument in its favour. One day, while tapping a hydrocele I laid gently hold of the testicle, and touched its surface lightly with the canula. The patient at once winced with pain and placed his finger unerringly over the place I had touched. A few days later another patient consulted me. His right scrotum was distended with fluid which I took to be a hydrocele. On tapping the sac I wished to demonstrate to a colleague the sensitiveness of the testicle. I laid hold of the organ and scratched lightly over it with the canula. The patient felt no pain. I scratched again rather roughly yet no sensation was felt. After removal of the fluid the swelling had not altogether subsided, and, suspecting what was the matter, I persuaded the patient to be operated upon. On opening the sac I found that the case was not one of hydrocele, but was a case of omental hernia with the hernial sac greatly distended by peritoneal fluid. In the case of the hydrocele I had been touching the sensitive surface of the tunica vaginalis, in the other case I had been scratching the insensitive surface of the peritoneum. As the origin of the tunica vaginalis is identical with the peritoneum this difference in sensation appeared strange to me. When, however, I looked up the nerve supply of the testicle I found it stated that the genital branch of the genito-crural nerve is distributed to the tunica vaginalis. This I hold to be a very striking testimony in favour of the definition. The tunica vaginalis, I believe, is the only serous membrane that receives a cerebro-spinal nerve, and the tunica vaginalis is the only sensitive serous membrane.

In certain cases the tunica vaginalis becomes hyperæsthetic. The pain from renal calculus, as is well known,

shoots into the testicle. As a matter of fact, it is in the tunica vaginalis that the pain is felt. This is readily shown, as in many cases the covering of the testicle becomes exceedingly sensitive to the lightest touch, while the tissues of the scrotum are not tender. Very frequently there is also an area of hyperæsthesia over the lower part of the abdomen, on the same side, in the field of distribution of the twelfth dorsal nerve, or upper lumbar nerves. The nerve supplying the tunica vaginalis comes from the upper lumbar nerves. The tissues of the scrotum, on the other hand, being supplied by the sacral nerves, are never hyperæsthetic in renal calculus. So distinctive is this hyperæsthesia of the tunica vaginalis that I have come to look upon it as a diagnostic symptom in doubtful cases of renal calculus.

XI.—The Mechanism by which the Sensory Symptoms in Visceral Disease Arise.

The manner in which the sensory symptoms in visceral disease arise has been described by several writers in dealing with referred pain. The stream of energy that passes to and from the viscera and spinal cord, as a rule, do not excite any consciousness in the subject. When from any cause an excessive stimulus passes from the viscera to the spinal cord, an excitation of the centres of other nerves occurs. As a consequence of this excitation, certain phenomena arise, according to the nature of the functions of the centres stimulated—it may be in the excessive action of some secretory gland; it may be in such a complicated reflex as vomiting; it may be in strong muscular contractions; it may be in such sensory symptoms as pain and hyperæsthesia. These symptoms may appear in parts remote from the organ in which the stimulus arises.

There is one other point in regard to pain and hyperæsthesia that merits some consideration. The impressions that pass from an area of hyperæsthetic skin reach the cord, while the sensory centres are in a disturbed condition. The result of the stimulus is very different from that which would have arisen under normal circumstances. What

would have been recognised in health as a touch gives rise to the sensation of pain. The point I wish to emphasise is this. Stimuli arising from other organs that usually pass unnoticed may give rise to the sensation of pain when the sensory centres are thus disturbed. A patient with marked cutaneous hyperæsthesia over the upper part of the abdomen, due to gall-stone colic, felt severe pain on the ingestion of food into the stomach. The history of the patient showed there had been no actual stomach lesion. With the disappearance of the cutaneous hyperæsthesia the gastric pain disappeared. It seems that in such a case the stimuli arising from the ingestion of food, which ordinarily passes unperceived, reach the cord while the sensory centres are in an intensely excitable condition. The stimulus has, therefore, an exaggerated effect upon them, and as a result pain is manifested in the peripheral distribution of their nerves. I mention this to illustrate the fact that the functions of one organ may give rise to pain, while the actual lesion is situated in an organ more or less remote.

XII.—Some Theoretical Considerations.

If the definition I have enunciated becomes established it will necessitate the modification of some of the views held in regard to the relationship of the sympathetic and cerebro-spinal nervous systems. In Quain's Anatomy it is stated that the sympathetic nerves and ganglia are merely outgrowths of the cerebro-spinal nervous system. The following train of reasoning arising out of the facts I have detailed to-night suggests that on the contrary the sympathetic system may be the older, and that the cerebro-spinal system is built up in the first instance for the protection of the sympathetic. I think it may be taken as a fairly well-established fact, that the more recent the development of an organ the more liable it is to be affected with disease compared with older established organs. This statement has been elaborated by several competent writers in regard to disease of the nervous system, and the proneness of the cerebro-spinal system to disease

has been compared to the comparative immunity of the sympathetic from gross lesions. But I should like to present a similar idea in a different form. In the administration of certain drugs, as chloroform, the manner in which they invade the system seems to be by a process of selecting the most recently-acquired functions, the one after the other. If, in the administration of chloroform, the process of abolishing all the more recent functions can be carried out until we produce a total suspension of the sensory and voluntary muscular systems, so far as they are dependent upon external stimulation, while the vital functions, as evidenced by the movements of the circulation and respiration, continue. In these functions the sympathetic system is largely employed, and it continues its work uninterruptedly while the greater part of the functions of the cerebro-spinal system is in abeyance. I have already remarked on the continuation of the muscular contraction under chloroform anæsthesia, when the stimulus producing this contraction arises from stimulation by means of a sympathetic nerve. The voluntary muscles engaged in the movements of respiration are still active so long as the stimulation reaches them from the viscera. Such a view suggests the following speculation. In the early development of animal life there is first evolved a digestive cavity, then later a rudimentary circulatory system. To these is added a rudimentary respiratory system. To co-ordinate these different systems, a nervous communication is developed which I suggest is the basis of the sympathetic system. The various organs are protected first by an insensitive, and, it may be, a somewhat unyielding outer covering. As development proceeds, this outer covering becomes modified in such a manner as to provide for both protection and movement. Then arises the sensori-muscular system. Protection is secured by rendering the outer covering sensitive, and by intimately connecting the sensory nerves with the muscles in what we call reflexes. In this manner, painful stimuli excite the muscle to contract, so that the organism is thereby removed from the offending neighbourhood. That such a view is probable, is seen in the development of the testicle. When this organ is cast forth

from the protection of the abdominal wall, it is provided with an extremely sensitive covering. The tunica vaginalis like the cornea, produces with the lightest stimulation only the sensation of pain. The nerve supplying the tunica vaginalis is associated in its origin in the spinal cord with the nerves supplying the powerful psoas and iliacus muscles, so that the lightest stimulation of the tunica vaginalis provokes the immediate contraction of these muscles, and the removal of the organ from the cause of offence.

Such, in brief outline, and in a somewhat desultory fashion, is the result of my observations. I could amplify the examples indefinitely from observations drawn from other organs, but as no mere statement of mine will finally establish the truth of this definition, I refrain from elaborating the argument, leaving it to each observer to find out whether the facts are as I have stated.

Reviews.

(1) *Care and Treatment of Epileptics.* By WILLIAM PRYOR LETCHWORTH, LL.D. New York, 1900.

(2) *Transactions of the National Association for the Study of Epilepsy and the Care and Treatment of Epileptics*, vol. i. Buffalo, 1901.

THESE two volumes are an outcome of the great and increasing interest in the welfare of epileptics which is manifesting itself in the United States of America. The work by Mr. Letchworth, who is a Past President of the New York State Board of Charities, gives a complete account of the epileptic colonies in Europe and America, and a valuable chapter upon the general principles which should guide those more immediately concerned in the development and management of such institutions. The work has required an immense amount of investigation and care in its construction. All the existing colonies on this side of the Atlantic have been visited, and important information given upon each of them. Largely as the result of the interest which many physicians in the States and others have shown in the colony treatment of epileptics, and fostered by the publication of articles in medical journals and by the direct appeals from Boards of Charities, it was decided in 1898 to form a National Association for the Study of Epilepsy and the Care and Treatment of Epileptics. This Association held its first meeting in Washington last year, and we have before us the published Transactions. The volume contains a number of interesting papers dealing largely with the colonies and special institutions existing in the United States, and two papers deal especially with the provision for the care of epileptics in the United Kingdom, and an account is given of the Chalfont colony, in Buckinghamshire, which is the property of the National Society for the Employment of Epileptics. It may be pointed out that neither of these volumes is, or contains anything in the nature of, a medical treatise upon epilepsy; but that they record observations and information respecting the history

and work of existing institutions for the treatment and care of epileptics.

In connection with these two volumes, a few words may be said upon the general principles involved in the treatment of epileptics in colonies, and to consider how far they are likely to exist as independent institutions. It is, however, quite necessary at the outset to point out that the general principle involved in the foundation of colonies for epileptics should be the care, management and treatment of the sane as contrasted with the insane epileptic. But it is well known that owing to the close relationship between epilepsy, idiocy and imbecility in early life, and with dementia in the later years, it is not always possible to draw any strict line of demarcation. There are, however, numerous epileptics visiting the out-patient rooms of the general and special hospitals, and in the wards of the Poor Law infirmaries, who, if suitable opportunities were afforded them, would be capable of contributing to their maintenance. The great mistake seems to lie in depriving the epileptic child of preliminary education. In this respect the epileptic is at a disadvantage compared with the blind, deaf mutes, and feeble-minded and defective children. The epileptic is in this predicament: unless he becomes insane or is from the outset feeble-minded or becomes a pauper, neither charity nor the State makes any provision for his maintenance. It is from the consideration of such facts as these that attempts are being made by various institutions, charitable and other, both in this country, on the Continent and in America, to do something to assist the confirmed epileptic. The solution of the problem is the foundation of colonies for epileptics. Into these institutions are taken epileptic children, with the view of affording them an education in accordance with the peculiarities of their affliction, epileptic youths and adults, with the object of providing them with employment of a kind specially suitable to their disease; and epileptics convalescent either from ordinary acute illness or from the immediate effects of their peculiar malady.

As already mentioned, the epileptic has not yet earned the protection of the State, but there exist several ways by which an epileptic colony may be satisfactorily financed. The first place is given to private benevolence; secondly, as the education of epileptic children is as much a matter for the educational authorities as that of normal individuals, and as it is in the majority of cases advisable that epileptic children should be educated apart from the non-epileptic, and preferably in colonies for epileptics, School Boards may legitimately contribute; thirdly,

as epileptic colonies may relieve the Poor Law authorities of able-bodied epileptics detained in workhouse infirmaries, the guardians should have the power to pay for such persons in epileptic colonies, as well as to assist relatives to maintain an epileptic member of their family in one of the colonies without at the same time pauperising such individuals; and, fourthly, by payments from the colonists. So far colonies have only been provided for the poor, or for persons of small means; but if this system comes to hold its own as the most satisfactory method of dealing with confirmed epileptics, it will be necessary to provide accommodation for those for whom high payments may be made.

It may be fairly claimed for the colony system that it provides the most satisfactory means of dealing with epileptics, both in the earlier stages of the disease and when it has become confirmed. The effect of removing the young epileptic temporarily from the ordinary occupations of life and placing him under the influence of the colony system would seem to be productive of much good towards the amelioration of his condition. The experience at the Chalfont colony in this connection has not been sufficiently extensive to permit of definite statements being made, but our observations would point to highly satisfactory results as likely to accrue from this method. The colony system is also of immense general value, for it offers the means of employment to a class of the community who have difficulty in finding work on account of their malady. It provides that kind of occupation which is most suitable for the nervous condition associated with the disease, as the work performed is scheduled and under direct supervision. The least active or alert have a fair chance of success, and perhaps of most value is the general salutary influence of the system upon the individual colonist.

From the interest which is taken in the colonies for the care and management of epileptics, full details of which will be found in the two volumes heading this review, it is the opinion of the writer that the system has "come to stay."

WILLIAM ALDREN TURNER.

Anatomie des Centres Nerveux. Par J. DEJERINE, Professeur Agrégé à la Faculté de Médecine de Paris; Médecin de la Salpêtrière; Membre des Sociétés de Biologie, de Neurologie, &c., &c., avec la collaboration de Madame Dejerine-Klumpke, Docteur en Médecine; Ancien interne des Hopitaux de Paris; Membre de la Société de Neurologie; Laureat de l'Institut et de l'Academie de Médecine. Tome ii., fascicule i. Anatomie du Cerveau (*suite*), Anatomie du Rhombencéphale. With 465 figures in the text, 180 of which are coloured. (Paris, J. Rueff, Editeur, 106, Boulevard Saint-Germain. 1901.)

THE first volume of Professor Dejerine's great work on the anatomy of the nervous centres was published in 1895. After several introductory chapters on the methods of study and development of the nervous centres, and on the general histology of the nervous system, it was occupied with the morphology of the cerebrum, with the study of microscopic sections of the cerebrum, with the structure of the cerebral cortex and its association and commissural fibres. The present volume is devoted to the consideration of (1) the projection fibres of the cerebral cortex; (2) the connections of the infra-cortical, or basal ganglia; (3) the olfactory and optic nerves; and (4) the rhombencephalon, or that part of the brain which stands in relation to the fourth ventricle. These various sections are studied on much the same plan as was adopted in the first volume.

The projection fibres of the cerebral cortex—*i.e.*, those fibres which, taking origin in the cells of the cortex, terminate at various lower levels of the central nervous axis—are considered with great fulness of detail, which is based upon the examination of no less than fifty-three cases of secondary degeneration. Three hundred pages and two hundred and forty-nine illustrations are devoted to this subject, which even yet is not fully completed. Only those fibres which terminate in ganglia situated above the pons varolii, and those paths towards lower centres which are found above that level are considered, the further continuation of these paths and their connections within the rhombencephalon and spinal cord being relegated to the volume which is to follow. In a most minute and masterly analysis these paths are traced through the centrum ovale, the internal capsule, and the cerebral peduncles. Definite portions of the optic thalamus

are proved to be connected with definite areas of the cerebral cortex, and an important addition has been made to our knowledge of the connections with the corpus striatum, the geniculate and quadrigeminal bodies, and the ganglia of the subthalamic region. The pes pedunculi, similarly analysed, is shown to consist entirely of fibres derived directly from the middle sector of the cerebral cortex—that is to say, the Rolandic area and the greater part of the temporal convolutions, the bundle of Türck arising entirely from the latter. These peduncular fibres have no origin from the corpus striatum. This section is illustrated by the detailed examination of a large series of brains, some with extensive, others with limited degenerations of cortical and subcortical areas, and of other brains which have been imperfectly developed; and the section is brought to a close with a discussion of the question of cerebral localisation, and with the projection fibres of the olfactory lobe.

The connections of the corpus striatum, the optic thalamus, and the subthalamic region are considered very fully, one hundred and five pages being devoted to them. The olfactory and optic nerves are treated in a chapter by themselves, apart from the other cranial nerves, as they form definite prolongations of the cerebrum itself. One would readily have welcomed an even fuller account of the optic nerve and its connections than the author has seen his way to furnish.

The concluding chapters are devoted to the study of the topography, structure, and texture of the rhombencephalon. The topography structure of the cerebellum is treated most exhaustively, and very fully illustrated.

The volume under review, the scope of which has thus been briefly indicated, more than fulfils the anticipations founded on the study of its predecessor, and which were expressed by the present writer in BRAIN, vol. xix. It is no exaggeration to say that, alike in its fulness and masterly handling of detail, and in the number, artistic excellence, and scientific accuracy of its illustrations, it stands unrivalled among books on the subject. One who has mastered its contents, especially with the aid of sections such as these figured so largely, will have a very complete knowledge of the anatomy of the brain. Fine as were the illustrations in the first volume, they are much surpassed in technique of drawing and in the manner of reproduction by those of the present one. The majority of the drawings are original, and have been made by the aid of a camera lucida from preparations of the author's. A personal opportunity

for comparing these drawings with the originals enables the present writer to speak to their marvellous accuracy. Professor Dejerine has done wisely to prefer this method of illustration to the false precision of photography.

Its author and his distinguished collaborateur, Madame Dejerine-Klumpke, are to be congratulated on the production of such an exhaustive work, which, in the writer's opinion, is destined to become the classic on the subject. It ought to form part of the equipment of every neurological and anatomical laboratory.

ALEXANDER BRUCE.

La Forme Spasmodique de la Syringomyélie, la névrite ascendante et le traumatisme dans l'etiologie de la syringomyélie. Par le DR. GEORGES GUILLAIN. (Published by G. Steinheil, 2, Rue Casimir-Delavigne, Paris, 1902.)

THE first portion of this work deals with a form of syringomyelia which the author considers has special claim to be recognised as a definite type and to which the adjective spastic has been attached. But although this spastic form of syringomyelia with its clinical features has not been described, the author fully recognises that certain spastic phenomena have not escaped the attention of neurologists.

Critzman describes this form of syringomyelia as resembling amyotrophic lateral sclerosis and other authors have described similar cases, but although the condition has been recognised pathologically, yet authors have not associated it with a definite clinical picture.

Five cases of this form are described with an autopsy and pathological investigation in two. The general attitude assumed by these patients is very characteristic: the arms hang parallel with the trunk, the fore-arm more or less flexed on the upper arm, the hand held in front of the pubis; the shoulders are raised, pushed somewhat forward; the head inclined forward. The external border of the trapezius often stands out very markedly and the supra-clavicular fossæ are deep; the whole attitude suggests

one of rigidity and is similar to that seen in paralysis agitans. Special attention is directed to the position of the hand, which is said to resemble that assumed by the preacher. The hand is dorsi flexed on the fore-arm, the three last fingers flexed into the palm of the hand while the index finger is more extended.

If, in association with the position above described, there is very marked loss of power in the upper and lower limbs with exaggerated reflexes and thermo-anæsthesia, the diagnosis of the spastic form of syringomyelia is clear.

The author discusses the differential diagnosis from amyotrophic lateral sclerosis, from fracture dislocation, from caries or cancer of the vertebræ. He does not consider that a differential diagnosis can be established between a cervical pachymeningitis and the spastic form of syringomyelia, for the two conditions may be present at the same time and due to the same cause.

The diagnosis from syphilitic myelitis is fully discussed and especial emphasis is placed upon the points to which Marie has called attention. It is, however, rare to find a syphilitic meningomyelitis in the cervical region.

Chapter VI. is devoted to pathological anatomy and figures and detailed description are given of the spinal cord in two cases. The degeneration of the crossed pyramidal tracts is very marked. The affection of the cord is most marked in the cervical region and here the posterior columns are almost completely destroyed.

The author, therefore, considers that both from a clinical and pathological standpoint, a spastic form of syringomyelia may with justice be described.

The second portion of the paper deals with the part played by an ascending neuritis and traumatism in the etiology of syringomyelia—for it may be said that although the symptoms and pathological anatomy are relatively well-known, the etiology of the disease is practically unknown.

The author expresses the opinion that affection of the spinal cord may take place by way of the peripheral nerves—*i.e.*, an ascending neuritis may cause a syringomyelia, and also that traumatism plays an important part in the origin and course of certain cases of syringomyelia.

With regard to the effect of ascending neurites, the following case is recorded: A man, aged 29, previously healthy, pricked his left hand, and an abscess developed. During the following year, progressive muscular atrophy of the hand, forearm, and arm developed. When 37 years old, he was examined by Madam Dejerine-Klumpke, who at that time found muscular atrophy of

the hand, forearm, arm, and shoulder, with alteration of sensibility to pain, and temperature in the hand and forearm. Twelve years later he was again examined, and at that time there was marked scoliosis, deformity of the thorax, atrophy of the hand, forearm, arm, and left shoulder, with trophic changes in the skin, and there was thermo-anæsthesia not only of both upper arms, but also of the trunk. The diagnosis of syringomyelia seemed certain, and in considering the various phases of the affection, how, little by little, the neuritis, secondary to the suppuration in the hand, ascended to the brachial plexus and to the spinal cord, it may with reason be suggested that a syringomyelia was thus developed.

There is in this case a typical example of the propagation to the cord of the inflammatory process by way of the peripheral nerves.

Numerous other cases reported by various authors are cited, proving the same point—viz., that syringomyelia may follow on peripheral injury. Some experimental evidence is then quoted, which is by no means so convincing as the clinical observations.

Siesler applied caustic to the sciatic nerve producing a complete paralysis, which terminated in the death of the animal, and at the autopsy a focus of inflammation was found at the point of emergence of the sciatic. A. Marie has shown that if a certain dose of tetanus toxine be injected into the sciatic nerve of an animal, a fatal result ensues, while, if previous to the injection of a similar dose of tetanus toxine, the nerve be divided, the fatal result does not occur.

The lymphatic circulation of the peripheral nerves is distinct from that of the surrounding tissue, and it seems to be well founded that there is a close anatomical connection between the lymphatic circulation of the nerve and that of the cord, and this explains the possibility of an infection of the cord by way of the peripheral nerves, and the author considers that he has demonstrated the possibility of a syringomyelia following on a peripheral infection.

Passing to the second etiological factor—viz., the effect of injury in the production of syringomyelia, numerous cases are quoted in which symptoms developed, as a direct effect of some traumatism.

The important work of Minor, who has shown that syringomyelia may follow on a hæmatomyelia is referred to, and also that of Van Giesson, who has given the name "hæmatomyelopore" to those cases with cavities of traumatic origin, in

which the symptoms are of sudden onset, and remain stationary, whereas in syringomyelia the symptoms develop slowly and are progressive.

The author believes that traumatism is a frequent cause of syringomyelia, but all cases of hæmatomeylia do not become cases of syringomyelia.

The question whether syringomyelia may be due to some obstetrical injury is next dealt with, and evidence is brought forward showing that the condition not infrequently occurs with difficult labour; but although the seat of this lesion and syringomyelia tends to be the same—viz., the cervical region, it cannot be asserted that such birth injuries are the cause of syringomyelia in later life. The presence of blood pigment in the wall of the cavity does not necessarily prove that the cavity is of hæmorrhagic origin, for hæmorrhage may occur into a syringomyelic cavity.

The author believes that the *rôle* which traumatism plays in the production of syringomyelia in some cases is as clear as the part played by ascending neuritis in the production of syringomyelia in others; and these conclusions are not only of theoretical interest, but have a very real importance from a medico-legal point of view.

FREDERICK E. BATTEN.

A Text-book of Insanity. By CHARLES MERCIER. (London: Swan Sonnenschein, 1902. Small 8vo, 6s.)

THIS book presents the usual characteristics of Dr. Mercier's work, keenness and originality of thought, closeness of reasoning, and perfect clearness of style. The distinction which the author always shows is present here in full measure. Coming as it does immediately after his longer work, "Psychology, Normal and Morbid," we expect it to be a practical supplement to that work. In the preface we are told that this little book is intended for students whose guides in this subject have hitherto been too bulky and voluminous. "Moreover," says the author, "I was anxious to put forward the distinction that I have drawn in this book between forms of insanity and varieties of insanity, a distinction which, I think, goes far to solve the difficulties of classification."

The book is divided into three parts: The Institutes of Insanity, Forms and Varieties of Insanity, and Legal Relations of Insanity. The first part deals in four chapters with Conduct, Mind Certifiability, and Causation. The author insists upon the importance of conduct. "Special stress," he tells us in the preface, "is laid upon observation of conduct, which is, in my opinion, the key to the subject." Again in the introduction—"Conduct is the main thing that is disordered in insanity." The statement is no doubt true and it is important, chiefly because it seems to keep the observer to plain practical points; but if we give, as Dr. Mercier appears to do, the fullest extension to the term conduct and make it cover not only, like Matthew Arnold's morality, three-fourths of life, but really the whole scene of human activity, it is open to question whether the generalisation is not too large for practical use. A very able analysis of conduct begins with the statement, "Conduct is the pursuit of ends,' and goes on, "All life is teleological, and the great end to which all life is directed . . . . is the continuation of the race to which the individual belongs," the self-preservative activities coming next in importance. It would, perhaps, bring us too far afield if we were to ask whether the "end" of life, in this sense, can be its mere continuance, racially or individually, since the acceptance of this view—is it not merely to place the elephant on the tortoise once more? And, besides, in the long history of our earth innumerable races of living things have ceased to exist just as individuals cease to exist. Therefore, the "end" of life cannot be racial continuance any more than individual existence; the "end" of life, apparently, is the continuance of life—the existence of life—life, and so our teleological circle ends where it began. But it is more important to see that the keen reasoning of Dr. Mercier on these great philosophic points is, in a somewhat different sense, teleological. It is the explicatory reasoning of the philosopher who contemplates, as it were, from the outside, the trend of events. "Conduct is the pursuit of ends." If this means cosmical or even racial ends, it is no doubt in the widest sense true, but it seems to lead us, as Carlyle used to say, nowhither. Applied to the individual, on the other hand, the motive force of life is not the pursuit of ends. Will, desire, impulse, are not to be so explained, and while the philosophers tell us that happiness is our being's end and aim, or that the continuance of the race is the end of individual life, man, who in action is quite unconscious that he is the conduit-pipe for the stream of tendency, acts as he wills—"so fondly he believes."

In other words, there seems to be a double meaning in Dr. Mercier's description of conduct and of the great "end" of life. It would perhaps be truer to say that conduct is the endeavour to fulfil desire, though there is probably a fallacy here too.

The second, and very much the larger part of the work, is given to forms and varieties of insanity. As we have seen, the author considers this distinction of high importance. "A form of insanity corresponds with what is called, in ordinary medical phraseology, a symptom; a variety corresponds with what is called a disease." The forms of insanity are, (*a*) weakmindedness, (*b*) stupor, (*c*) depression, (*d*) excitement, (*e*) exaltation, (*f*) suspicion, (*g*) systematised delusion, (*h*) obsession and impulsiveness, (*k*) moral perversion. The varieties, (1) idiocy and imbecility, (2) dementia, (3) stupor, (4) acute delirious mania, (5) acute insanity, (6) fixed delusion, (7) paranoia, (8) *folie circulaire*, (9) insanity of reproduction, (10) insanity of times of life, (11) insanity of alcohol, (12) general paralysis, (13) insanity of epilepsy, (14) insanity of bodily disease.

It is not easy to see how this classification is an improvement upon several of the earlier attempts. To the writer of this review, it appears only to emphasise the difficulty of the question. In his preface, Dr. Mercier says: "I hold that there are not insanities but insanity only." Therefore, a form and a variety cannot be very distinct. In his divisions "stupor" actually occurs under both rubrics. In what sense is "dementia" a variety comparable to general paralysis? The description of dementia is chiefly applicable to a secondary state. It seems, therefore, inappropriate to class it as anything corresponding to a disease. The section upon dementia concludes thus: "The only form of dementia which has a true clinical distinctness, and constitutes a separate clinical entity, is that which is known as stupor." One might, therefore, be justified in supposing that the "variety" called "dementia" is not a clinical entity. That an author so acute and logical as Dr. Mercier should thus be entangled, appears to show that the difficulty of classification is at present insoluble. The old objection to eclectic classifications, that they are formed by adding together things that have no common denominator, seems to apply. Again, the objection that some varieties are very distinct, and others are mere "refractory wards" cannot be altogether avoided where such divisions occur as "acute insanity" and "dementia." The difference made between "fixed delusion" and "paranoia," that in the former "the delusion has practically no effect upon conduct," would

appear to be only a question of degree. Though an excellent description is given of senile dementia under the heading "dementia," yet where it is referred to under causation, and under the heading "insanity of times of life," it is not sufficiently distinguished from other conditions of mental aberration occurring in old age. Yet it would appear to the writer of this notice, that there is no variety of insanity which is more distinct than senile dementia, distinct in symptoms, in course, and in pathological anatomy. The classification cannot be perfectly natural which associates this incurable organic disease of the brain with other conditions occurring, indeed, in old age, but often quite curable.

In a chapter of the highest excellence on the causes of insanity, Dr. Mercier discusses, among other things, the question of vulnerability, predisposition, heredity. Wisely, no doubt, he has not returned to this point with regard to classification, for the Continental authors who have endeavoured to differentiate hereditary and degenerative insanity do not seem to have fully proved their thesis.

The last part of this book, which treats of the legal relations of insanity, is probably sufficient though short, and deals with this intricate subject in a very clear and able way.

In his preface, the author has, as it were, challenged criticism on certain points on which we therefore dwell, and, as they are moot points, freely express dissent. But his claim to credit for brevity must be admitted, and no critic can but admire his terseness and vigour, and the clear emphatic style so valuable in a book for students.

Space does not allow of reference to the numerous keen and original observations scattered through the volume. Treatment is not separately dealt with, but many valuable therapeutic notes appear throughout. "Neurologists," says Dr. Mercier, "who are frequently consulted about cases of insanity, though it is a subject of which they have no special knowledge, almost invariably advise that the patient should travel. . . . Travelling is, however, almost always detrimental in the early stages of insanity." Perhaps he might have gone a little further, and referred to cases of acute melancholics who ought to be in their beds, and who are trotted round to various diversions till they are driven to suicide or worse, to incurability.

CONOLLY NORMAN.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

A paper by Dr. James Mackenzie on "Pain" was read before the Neurological Society on October 23, 1902, and appears at p. 368 of the present issue.

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